DOES NOT CIRCULATE

ACTA RADIOLOGICA

CONDITA A GÖSTA FORSSELL

EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE ET SUECIAE

Editor ERIK LINDGREN, Stockholm / *Editor adiuvans* OLLE OLSSON, Lund

Redactores

Dania: P. Flemming Möller, Köbenhavn; C. Krebs, Århus
Fennia: G. Jansson, Helsingfors; S. Mustakallio, Helsingfors
Norvegia: T. Dale, Oslo; J. Frimann-Dahl, Oslo
Suecia: S. Hultberg, Stockholm; F. Knutsson, Upsala

UNIVERSITY OF MICHIGAN
SEP 24 1954
MEDICAL

INDEX

The relationship between the third ventricle and the basilar artery. By *T. Greitz* and *S. Löfstedt* 85
The cervical spinal canal in intraspinal expansive processes. By *Erik Boijsen* 101
Free gas in the fetal vessels as a roentgenologic sign of intra-uterine fetal death. By *Olov Fr. Holm* 116
On the tolerance of the rabbit's kidney to contrast media in renal angiography. By *Hans Idbohrn* and *Nils Berg* 121
Unusual coronary branch in a case of coarctation. By *L. Di Guglielmo* and *M. Guttadauro* 141
Carcinoma of the paranasal sinuses and the nasal cavitities. By *Lars-Gunnar Larsson* and *Gunnar Mårtensson* 149

VOL. 42 AUGUST 1954 Fasc. 2

ACTA RADIOLOGICA

EDITORIAL NOTICE

ACTA RADIOLOGICA publishes original papers relating to medical radiology and nuclear medicine. The articles are printed in English, French or German according to the wishes of the author. Contributions from all countries are accepted but priority is given to those from Scandinavian sources. Papers are published on the clear understanding that they are contributed exclusively to Acta Radiologica. They are subject to editorial revision and the right is reserved to introduce such changes as may be necessary to make the contributions conform to the editorial standards but Acta Radiologica does not hold itself responsible for any statements made or opinions expressed by authors. Contributions should be as concise as possible. Papers of more than 24 pages, including space for figures and tables, cannot be accepted for publication without special permission from the Editor. More extensive articles may be published as supplements at the author's own expense. These are not subject to editorial revision. Manuscripts from Denmark, Finland and Norway should be forwarded to the Sub-Editors of the respective countries, and other manuscripts direct to the Editorial Secretary, Acta Radiologica, Stockholm 2, Sweden.

Manuscripts must be typewritten with double spacing (at least 1 cm between each line) and adequate margins and a short summary should be included with each. All manuscripts should bear the name and full address of the contributor. A copy of the manuscript should always be retained by the author so that it may be available in the event of the original being lost in transit. Alterations to print are costly and, with the exception of small corrections, will be charged to the author. Footnotes should be avoided as far as possible, since they break the reading of the text and are expensive.

Illustrations and tabular material should be unmounted, and attached to the manuscripts in an individual cover. Numbering should be indicated in pencil lightly on the back and never appear on the front. The illustrations must be provided with suitable short legends and so worded that they are comprehensible without reference to the text. These legends should be typewritten on a separate sheet and not under the respective figures. Care should be taken that the illustrations only show the necessary details and essential features. Drawings and charts for reproduction should be in *black* (never in blue). The Editor reserves the right to reduce the size of illustrations as considered appropriate.

A bibliography must be added and the references should be arranged in alphabetical order of the author's name followed by his initials, full title of the paper and name of the journal — abbreviated according to *Fishbein: Medical Writing* or the *Quarterly Cumulative Index Medicus*. The volume number, year and number of first page of article should follow. Reference to books and monographs should indicate the author, the title, the edition, the name and city of the publisher, and the year of publication.

Example:

TILLINGER, K. G.: Papillary cystadenolymphoma. Acta radiol. 28 (1947), 241.

CAFFEY, J.: Pediatric X-Ray Diagnosis, Second Edition. The Year Book Publishers, Chicago 1950.

Fifty reprints will be presented to the author or divided among joint-authors. Additional reprints may be purchased at cost price but the necessary order must be given when the proof is returned.

Annual subscription rate 70 Swed. Kr. (plus 6 Sw. Kr. postage outside Scandinavia) payable in advance. (Two volumes, each of 6 numbers, appear annually.) Single copies 7 Sw. Kr. (plus postage Sw. Kr. 0:50) The subscription will be considered automatically renewed if not cancelled at the latest 10 days before the publication of a new volume.

All communications in regard to advertising, subscriptions, change of address, etc., should be sent to Acta Radiologica, Stockholm 2, Sweden.

ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE, ET SUECIAE

VOL. 42 AUGUST 1954 FASC. 2

THE RELATIONSHIP BETWEEN THE THIRD VENTRICLE AND THE BASILAR ARTERY

by

T. Greitz and *S. Löfstedt*

The anatomy of the floor of the third ventricle. The floor of the third ventricle consists of the chiasma, the tuber cinereum with the infundibulum, the corpora mamillaria, substantia perforata posterior and the peduncles. The substantia perforata posterior at the same time forms the roof of the cisterna interpeduncularis. In this cistern, frontally demarcated by the corpora mamillaria and tuber cinereum, the basilar artery is situated and divides into the two posterior cerebral arteries. There is thus a close relationship between the basilar bifurcation and the floor of the third ventricle which may be studied roentgenologically with the help of encephalography and angiography of the vertebral arteries. In order to be in a position to judge pathologic changes in the relationship between the basilar artery and the third ventricle, it is necessary to be acquainted with the variations in the normal roentgen anatomy.

The description of the appearances of the third ventricle in true lateral views as given in the literature is often vague, incomplete, and many a time incorrect. It has been most energetically maintained by LINDGREN in his work on the temporal horn, that there must be complete air filling of that part of the ventricular system to be examined. In order to get such a complete filling of the third ventricle that a true representation of the floor is obtained, the patient's head must lie with the brow well raised and the central beam directed horizontally. It is to be noted that the direction of the central ray and the position of

Submitted for publication, December 8, 1953.

From the Roentgen Department II (Director: Docent W. MAGNUSSON), Södersjukhuset, Stockholm, Sweden.

the head must be absolutely exact in order that true lateral views be obtained; even small deviations change the appearance of the floor of the ventricle. If the amount of air is insufficient to fill the ventricle in this position, hyperextension of the head will cause the air to lie against the floor. If encephalography after lumbar or suboccipital injection as described by ROBINSON and LINDGREN, is carried out on a patient in a sitting position, the posterior part of the ventricle will practically always be filled with air, even if only a small amount passes in intraventricularily. By comparing the films taken during the air insufflation with those mentioned above, a true conception may be obtained of the whole anatomy of the ventricle.

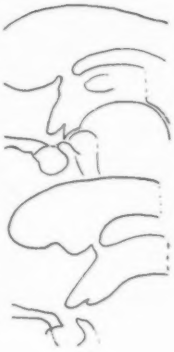
On the other hand, if the ventricular system is filled in one operation and lateral views with vertically directed rays are then obtained, the result will almost without exception be incomplete filling of the third ventricle, and the roentgenogram will give an incorrect conception of the anatomy. As mentioned, any lack of precision in the projection will bring about still further errors.

TWINING, in 1934, and independently of him, LYSHOLM in 1935, were the first to mention the technique of obtaining lateral views of the third ventricle with the head in an axial position (hyperextended) and the rays directed horizontally. But from what is to be found in the literature it is apparent that an incorrect method with vertically directed rays is still often used. However, in LYSHOLM's 'Das Ventriculogramm', the third ventricle is somewhat scantily treated. SAHLSTEDT, who wrote the chapter 'Das normale Ventriculogramm' states that the recessus opticus and the recessus infundibuli may be 'spitz ausgezogen oder breitbasig stumpf', but otherwise does not mention the floor of the third ventricle. A detailed description of the floor has been given by EPSTEIN as follows: "The floor of the third ventricle is variable in configuration. It may extend directly caudad as a relatively straight line inclined slightly upwards, or the floor posteriorly may be represented by a curvilinear upward convexity. If the degree of filling is poor, or if the walls of the third ventricle are close together, this apparent indentation may be exaggerated." To judge by EPSTEIN's description and illustrations, he employed lateral views taken with vertically directed rays. In our experience the floor of the third ventricle never has the appearance of 'a relatively straight line'. It is always more or less curved. EPSTEIN's conception is based on the fact that the lateral views were obtained with the rays directed vertically. With the head in this position, air-filling of the third ventricle may be incomplete. EPSTEIN's technique, which is also used by many others, requires, if a true representation of the anatomy is to be obtained, a complete exchange of fluid with air, which can practically never be obtained by encephalography or ventriculography. EP-

a. b.

c. d.

1 a. 1 b



1 c. 1 d.

Fig. 1. Normal cases. a) a child, three months old. The position of the anterior recesses is high above the entrance to the sella, the basal cisterns are wide, the aqueduct and the floor of the third ventricle forming a sharply curved arch. b-d) adults. b. The position of the anterior recesses is close to the entrance to the sella. Note the comparatively regular arch described by the floor of the third ventricle. The arrow points to the pocket between the corpora mamillaria and the infundibulum. c. The position of the anterior recesses high over the entrance to the sella. The pocket (→) is only slightly marked. The corpora mamillaria form a shallow impression in the floor. d. The pocket is missing as the corpora mamillaria do not bulge into the third ventricle.

STEIN's conception of the appearance of the third ventricle cannot therefore be accepted.

An unsatisfactory method of examination must also constitute the foundation for the statement that the third ventricle is normally so thin that it does not show in a lateral view, (among others HEIDRICH 1927 and SCHIERSMANN 1952). SCHIERSMANN says: "Gelingt die Darstellung aller Einzelheiten des III. Ventrikels, dann kann man mit grösster Wahrscheinlichkeit eine Erweiterung annehmen." To this may be added: When the roentgen technique is correct the third ventricle will always be visualized under normal as well as pathologic conditions, providing it can be filled with air. There is therefore no reason to carry out tomographic examinations as recommended by DAVIDOFF and EPSTEIN, and others.

In order to obtain a conception of the roentgen anatomy of the third ventricle and its variations we have studied its appearance from a material consisting of fifty ventriculograms and fifty encephalograms of adults (15—66 years of age) and of thirty encephalograms of children (2 months—14 years of age). These cases belong to a complete material of about 2,000 encephalograms and ventriculograms from our department.

The floor of the third ventricle from the mouth of the aqueduct to the recessus infundibuli in adults forms a curve, convex upwards (Fig. 1 b). The recessus opticus and infundibuli vary in form and size, as SAHLSTEDT has pointed out. Their positions also vary, both in the fronto-occipital and the basi-cranial directions. Thus they may be found in the immediate neighbourhood of the upper edge of the dorsum sellae, 1 cm or more directly above, or entirely in front of or behind it (Fig. 1 b, c, d). From a practical point of view it is important to note that the distance between the recesses and the entrance to the sella may be a full centimetre also in cases where no supracellar expanding lesion is present. In cases on the borderline that are difficult to judge, it is therefore of greater importance to consider the form of the anterior part of the third ventricle than to judge its distance from the entrance to the sella. In the front part of the floor of the third ventricle a small pocket is often, although not always, found; it is bordered frontally by the tuber cinereum and posterially by the curving corpora mamillaria (Fig. 1 b, c). In cases in which the corpora mamillaria do not bulge into the third ventricle this pocket will not be present (Fig. 1 d). It has, however, been described by SUTTON as a constant formation. The distance between the pocket and the recessus infundibuli may be longer or shorter according to the variations in size of the latter. The posterior boundary of this recess may be straight or form a convex curve forwards or backwards (Fig. 2). When it curves backwards the floor of the ventricle as a

Fig. 2 (schematic). Variations in the anterior part of the floor of the third ventricle with and without the recess described by SUTTON. Compare Fig. 1.

whole forms an S-shape. If the third ventricle and the basilar cisterns are simultaneously filled with air, that part of the wall made up of the tuber cinereum will be shown to be only 1—2 mm thick (Fig. 1 b). Posterior to the tuber cinereum the floor of the ventricle usually runs in an even, somewhat shallow curve, onto the mouth of the aqueduct. This curve may be more accentuated in its anterior part, corresponding to the corpora mamillaria which may sometimes form a sharply outlined impression, the size of a split pea. In the case of young children in the first years of life, the arch formed by the floor of the fourth ventricle, the aqueduct, and the floor of the third ventricle has a sharper curve, which is due to the fact that the base of the skull is comparatively short (Fig. 1 a). The frontal part of the third ventricle is thus in children directed basally, *i. e.* at right angles against the floor of the frontal base of the skull. In consequence a more or less acute angle is formed between the anterior and posterior halves of the floor of the third ventricle. The ventricle thus assumes the shape of a hook. We have made repeated encephalograms of children from five months to five years of age, and found that during growth this juvenile shape changes and the ventricle gradually takes on the usual adult appearance with a more flat and regular arch. The change in the form of the third ventricle which takes place during growth is probably connected with the relatively great increase in the length of the base of the skull during the first years of life. A prominent arch or hook-shape of the floor of the third ventricle in children under the age of five, is thus not pathologic but a usual and normal variation in form. However, an indication of the hook-shape is sometimes also to be found in adults. The third ventricle usually attains an adult shape as early as the age of four to five years. These roentgenologic observations agree with the findings of the anatomist DABELOW. In newborn infants the stalk of the pituitary body is directed basally backwards, while in adults it is directed basally forwards. The anterior recesses of the third ventricle are generally to be found at a greater distance from the base of the skull in children than in adults and consequently the basal cisterns are comparatively larger in size; this was also stated by PALMGREN in 1936.

The anatomy of the basilar artery. The cisterna interpeduncularis contains the basilar bifurcation, which according to LINDGREN is to be found

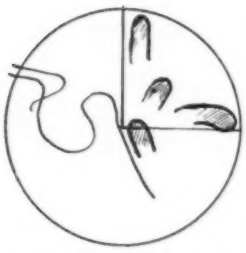
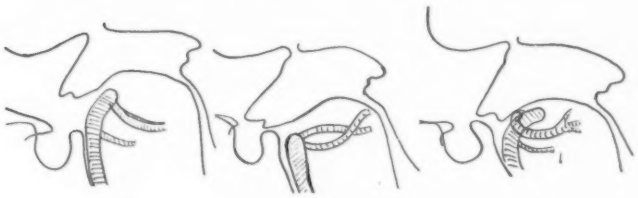


Fig. 3. Variations in the position of the normal basilar bifurcation.

'at the level of, or just above, the posterior clinoid process'. RADNER points out that 'the point of the basilar bifurcation varies in a sagittal direction 'and that it 'may be projected at the clinoid line or as high as 1 cm above this line'. As 'the clinoid line' cannot be roentgenologically determined, this localization becomes vague. In RADNER's treatise, (Fig. 61, p. 118), films are to be found that undoubtedly show pathologically distended basilar arteries, but this phenomenon was not discussed. According to LINDGREN the basilar artery as a whole may run parallel to the clivus, but in many cases its superior part bends off backwards in an arch which may be quite sharply curved. The position of the basilar bifurcation thus varies considerably in relation to the base of the skull. Out of a material of fifty vertebral angiographies from our roentgen department the bifurcation is to be found within a surface which, generally speaking, is constituted by a quadrant of a circle with a radius of 20 mm and its centre close to the dorsum sellae (Fig. 3).

Its relation to the floor of the third ventricle on the other hand is less variable. This relation we have determined in vivo by comparing the findings in pneumographies and vertebral angiographies when both examinations on different occasions have been made of the same patient. This has also been performed at autopsy by filling in situ the third ventricle with air and the basilar artery with contrast medium. (We have filled the third ventricle with air by puncture of the ventricle, and the vertebral artery with contrast medium, films being obtained without opening the skull.) The in vivo material consists of twenty unselected cases, and the sectional material of four cases. In addition, it has been possible to discern the basilar artery and its bifurcation from encephalograms of about twenty-five children and a somewhat lesser number of adults without injecting the vertebral artery; it has been possible to detect them in the airfilled cisterns. In cases in which the bifurcation is to be found high above the sella, the position of the third ventricle is also high — *i. e.*, at a greater distance from the base of the skull (Fig. 4 a). And in cases where the basilar artery is short so that the bifurcation lies at the same level as the point of the dorsum sellae, the third ventricle will also be found in a more basal position (Fig. 4 b). If the bifurcation is placed posterior to the dorsum, the third ventricle will be found in a more occipital position as well (Fig. 4 c). The basilar bifurcation has thus, in the case of adults, an almost constant position immediately behind the posterior part of the hypothalamus so that its distance from the nearest part of the third ventricle varies



a. b. c.

Fig. 4. Three cases showing the relatively constant relationship between the floor of the third ventricle and the basilar arteries. The drawings are copied from encephalograms and angiograms of three living subjects (not schematic). (a) The third ventricle in a high position — a long basilar artery. (b) The third ventricle in a basal position — a short basilar artery. (c) The third ventricle in an occipital position — the basilar artery bent backwards.

between 0 and 6 mm. These roentgenologic observations have been verified by studies in situ in more than one hundred autopsies. In the case of infants, where the cisterns often are comparatively voluminous, the relation between the third ventricle and the basilar bifurcation becomes less constant. The basilar artery often projects relatively further into the cavity of the skull than it does in adults; as in the case of the so-called hook-shape of the third ventricle, this is probably due to the relatively short base of the skull. It is thus evident that the appearance of the third ventricle and the basilar artery, as also the relationship between them, changes considerably during the first years of life.

The basilar artery impression into the third ventricle. As already pointed out in describing the relation between the floor of the third ventricle and the basilar bifurcation, the position of the latter varies considerably depending, either upon how far the basilar artery projects into the cavity of the skull, or upon the shape of the basilar arch. In five cases in which both encephalography and vertebral angiography were carried out, the position of the bifurcation was such that it deformed the floor of the third ventricle. (That this might happen has earlier been observed — LINDGREN, SJÖGREN — but has not been the object of a close study, as far as we know.)

Case 1. Male, aged 62, with a left-sided homonymous hemianopsia and clinically suspected of an expansive process in the right occipital region. Blood-pressure 210/150. On encephalography a limited and clearly defined impression into the middle of the floor of the third ventricle was noted. The expansive process lay directly opposite to the foramen Monro, so that the middle part of the third ventricle was considerably compressed from the basal aspect, and the parts of the third ventricle situated anteriorilly and posteriorilly to the compression together formed an acute angle. Thus the appearance of the ventricle somewhat resembled the so-called 'hook-shape' of children. How-

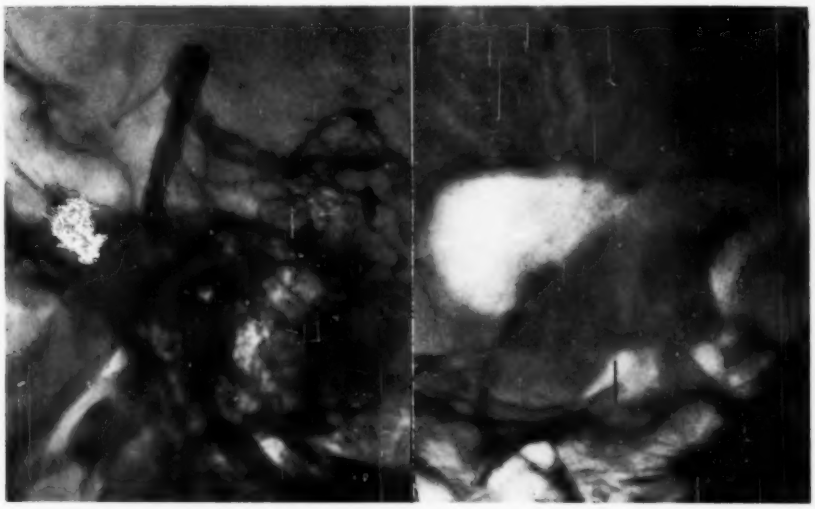


Fig. 5. Case 1. A well-defined impression in the middle of the floor of the third ventricle. The basilar artery is elongated but only slightly widened. Its lumen is irregular, pointing to arteriosclerosis. The distance between the floor of the third ventricle and the basilar bifurcation is due to the corpora mamillaria.

ever, owing to the compression it was of altogether another character. The cisterna interpeduncularis and the uppermost part of the cisterna pontis were but insufficiently filled with air, most likely due to unsatisfactory technique. The recessus opticus and infundibularis were well defined. The aqueduct was not deformed. Diagnosis: A comparatively small, well-defined, expansive process in the floor of the third ventricle or in the cisterna interpeduncularis and the uppermost part of cisterna pontis. In order to decide if the change was caused by a tumour or by an aneurysm close to or adjoining the basilar bifurcation, vertebral angiography was carried out. It was then observed that the deformation of the third ventricle was due to an unusually elongated and widened basilar artery. Its contours were irregular, pointing to arteriosclerosis; no aneurysm was found. Apart from moderate central and cortical atrophy no other abnormalities were noted.

Case 2. Male, aged 54, with suspected cerebral thrombosis, and paresis of the left arm and leg. Blood-pressure 215/130. On encephalography the same findings as in the previous case were made and vertebral angiography showed that the deformation of the third ventricle was also due to a very long and wide basilar artery; no aneurysm was discovered. In this case both the cisternae pontis and interpeduncularis were filled with air; both were unusually spacious, and in the cisternae the long and wide basilar artery could be discerned in its entirety. The recessus opticus and infundibularis and the aqueduct were not deformed.

Fig. 6. Case 2. Hook-shaped third ventricle. The basilar artery is elongated and widened.

Case 3. Male, aged 58, with attacks of headache, giddiness, vomiting, and a left-sided peripheric facial paresis. Blood-pressure 240/130. Encephalography showed a considerable deformation of the third ventricle which was of the same type as in the previous cases, but somewhat more marked. The recessus opticus and infundibularis and the aqueduct were also without any abnormalities. The cisternae pontis and interpeduncularis were comparatively well filled and the basilar artery could be defined, although not throughout its entire length. The anterior part of the third ventricle was displaced slightly laterally, and vertebral angiography showed the basilar artery to be very long, wide and tortuous, both in the frontal and sagittal planes. In a true lateral view it was partly projected into the third ventricle. Owing to a bend in the sagittal plane the basilar artery had the appearance of the handle of an umbrella, with the concavity turned backwards. Vertebral angiography was carried out immediately after the encephalography, so that the third ventricle was filled with air and the basilar artery with contrast medium in one and the same film.

Case 4. Male, aged 58, with weakness of the legs and a spastic gait. Blood-pressure 235/140. In this case the deformation of the basilar artery and the third ventricle had a somewhat different appearance from that in the previous cases. The deformity of the ventricle was decidedly more pronounced, and the impression in the soft tissues irregular. The anterior and medium parts of the ventricle were also displaced somewhat laterally, and the anterior part slightly forwards. The recessus and the aqueduct were not deformed. The basilar artery could be partly discerned in the cisternae pontis and interpeduncularis. Vertebral angiography showed that the basilar artery was longer and more tortuous than in the previous cases. Thus the position of the basilar bifurcation was not directly beneath the third ventricle, but somewhat to the side of it, so that

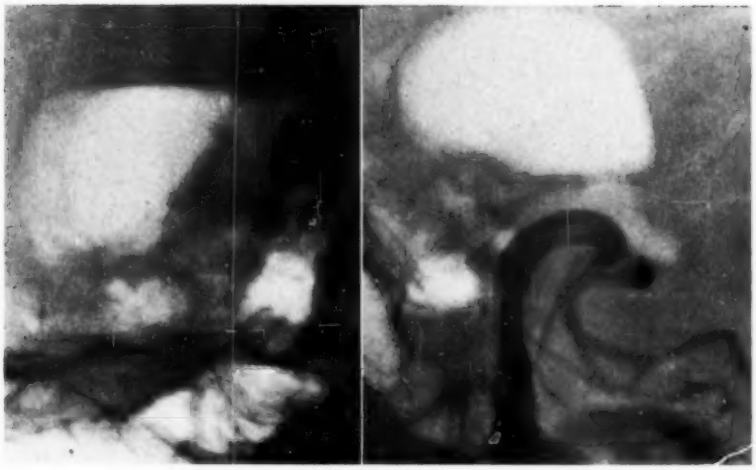


Fig. 7. Case 3. Vertebral angiography carried out immediately after encephalography. The basilar artery is very long, wide and tortuous with small intimal plaques. It is partly projected into the third ventricle, and looks like the handle of an umbrella, with the concavity turned backwards.

it projected into the third ventricle from below as well as from the side. The lumen was rather irregular. In the lateral view the basilar artery had the appearance of the handle of an umbrella, but in this case with the concavity turned forwards.

Case 5. Male, aged 52, with hypertonia, giddiness, weakness, attacks of unconsciousness and facial paresis. Blood-pressure 200/130. A considerable, somewhat irregular, impression of the soft parts in the floor of the third ventricle was noted, the rostral portion of the ventricle being protruded slightly forwards. In the medial part of the ventricle the soft tissue showing a well-defined small prominence, reached as far as the foramen of Monro, so that the ventricle was considerably compressed, without being entirely cut off. The deformation was more pronounced than in any of the previous cases. The recessus and the aqueduct were not deformed. The basilar cisterns were very wide, and in the cisternae pontis and interpeduncularis a long and wide basilar artery could be discerned. Vertebral angiography showed the basilar artery as being considerably prolonged, widened and tortuous, both in the frontal and sagittal planes. The deformation of the third ventricle corresponded to the basilar bifurcation and one of the posterior cerebral arteries, the latter being the cause of the extra impression adjoining the foramen of Monro. The fact that the posterior cerebral artery in this case took part in the deformation of the ventricle was in some degree due to the basilar artery being partially revolved around its longitudinal axis, and also to its unusual winding course in the frontal plane, so that the bifurcation had a markedly asymmetric position. The basilar artery presented an irregular lumen. In this case there was again the suggestion of an umbrella handle shape with the opening of the handle directed forwards.

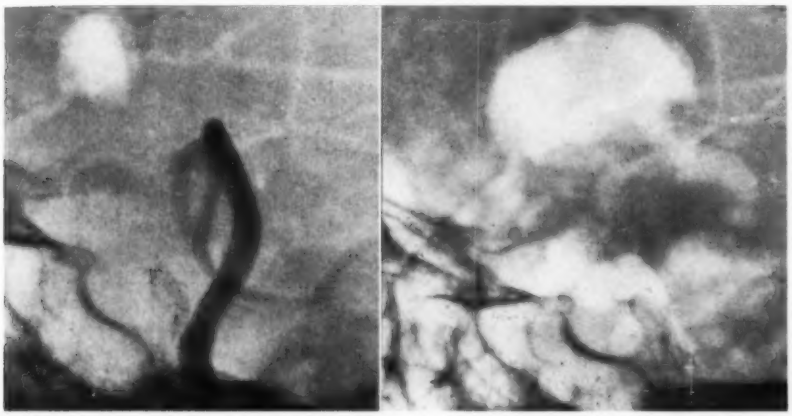


Fig. 8. Case 4. Irregular indentation in the floor of the third ventricle. The basilar artery is elongated and tortuous. Handle of an umbrella appearance but with the concavity turned forwards.

In all five cases a long and wide basilar artery thus caused a well-defined, oval—circular or irregular nodular impression in the floor of the third ventricle. This impression is so characteristic, that the diagnosis should be arrived at by encephalography. Craniopharyngiomas and tumours in the hypothalamus and pons may sometimes give a similar deformation. In the case of a craniopharyngioma, the rostral portion of the third ventricle with its recesses is also always deformed. Tumours that grow in the hypothalamus and pons, or protrude from the membranes in or around the basilar cisterns, compress or fill up the latter. In the basilar enlargement described above, on the other hand, the basilar cisterns were in all cases except one (the airfilling was insufficient, probably for technical reasons) unusually spacious. Encephalography is thus superior to ventriculography, in which air-filling of the cisterns is always incomplete. In any case angiography of the vertebral artery should always be carried out in order to verify the diagnosis and above all to decide if an aneurysm exists in the basilar bifurcation or its immediate neighbourhood. In these five cases the observations were made from a routine material (circa 600 encephalographies) extending over a period of two years. The change cannot therefore be so uncommon. In this connection it is to be noted that the imperfect methods of encephalography still used in many centres,

a. b.

c.

Fig. 9. Case 5. The middle of the third ventricle is almost completely compressed. The well-defined prominence reaching right up to the foramen of Monro is caused by one of the posterior cerebral arteries. The artery is markedly elongated, widened and tortuous with irregularity of the lumen pointing to intimal thickenings.

is probably one of the chief reasons that similar cases do not appear to have been described.

DANDY, amongst others, has called the generally enlarged basilar artery an aneurysm, which is unwarranted from a pathologic-anatomic point of view. To avoid any confusion with the congenital, sac-shaped aneurysms, which are neither surgically nor pathogenically identical, we have not used the term aneurysm for these changes in the basilar artery. Of course they cannot be surgically treated and are of interest only from a differential diagnostic point of view. The condition should be called an ectasia.

All five patients were over fifty years of age and had clinical as well as roentgenologic signs of advanced arteriosclerosis. The blood-pressure was considerably increased, the systolic pressure varying between 200 and 240 mm Hg. No calcification of the basal artery was visible in any of these cases. In two of them, carotid angiography was carried out; the carotid syphon was seen to be elongated and dilated, as was to a lesser extent the basilar artery. The size of the basilar artery varies in individual cases quite considerably, but it seems likely that pathologic changes (arteriosclerosis, or some other form of degeneration) and high blood-pressure are necessary in order to cause such extreme ectasia of the artery that the third ventricle becomes deformed.

The pathology of the basilar artery. Out of 200 brain sections performed, three cases were found with elongated and extremely dilated basilar arteries together with deformation of the third ventricle. In two of these cases the basilar artery lay in the midline with its superior part having the appearance of the handle of an umbrella. However, in the third case the basilar artery, both in the sagittal and frontal planes, was seen to pursue a markedly tortuous course. Its superior part did not show the typical umbrella handle shape. The bifurcation was situated to the side of the third ventricle and the deformation was not primarily caused by the bifurcation itself, but by one of the two posterior cerebral arteries (compare Case 5 of the material examined roentgenologically). It was most noticeable that the common irregular patchy sclerosis which occurs in arteriosclerosis of the basal brain-vessels, is usually combined with extreme changes in the intima. In advanced cases this gives the vessels the appearance of a string of pearls. The first two cases mentioned did not show this appearance. Instead, the basilar artery was as regular as a rubber tube but with a moderate and homogeneous thickening of its walls; the usual patchy sclerosis and changes in the intima hardly existed. The walls of the vessels, in spite of their thickness were not particularly hard, but soft and flexible. In the third case a pronounced patchy sclerosis and a considerable change in the intima was noted. In this respect it resembled the usual form of arteriosclerosis and was considerably widened, elongated and flaccid, as in the other two cases. Thus the vessel represents a different and special type, in spite of certain similarities to the so-called usual form of arteriosclerosis. It may be looked upon as a combination of the string of pearls and the rubber tube types.

In one of the two above-mentioned cases, in which autopsy was performed, a microscopic examination was carried out. The elastic substance was almost completely absent while in examinations of patients of the same age (of cases of the so-called string of pearls type) it has

been found intact, or in any case far less damaged. (The matter is being investigated and the results will be published later.)

GLYNN has shown, that of all the different tissues in the walls of the arteries, the elastic substance is of the greatest importance in the power of resistance against the expanding effect of the blood-pressure. He removed the muscle sheaths but retained the tunica intima and tunica elastica; he found that this caused little decrease in the power of resistance of the walls of the arteries to pressure. Thus, if the elastic substance is destroyed for some reason or other, and increased blood-pressure of a local or general nature occurs, this may cause widening and elongation of the basilar artery. The damage to the elastica is most likely of a more or less general nature. In all cases in which angiography of both the carotid and the vertebral arteries has been carried out, the arteries have been found to be widened, elongated and tortuous. The same observations have been made at autopsy. Several roentgenologists — especially of German nationality — have previously discussed the roentgen appearances in cases of arteriosclerosis, without entering into any discussion upon the different types of arteriosclerosis.

The necessary condition for the basilar bifurcation to reach far into the cavity of the skull, consists, of course, in it not being fixed in its ramifications; these must also be elongated, which they have proved to be in all the cases examined. Elongation of the basilar artery alone if both ends were fixed, would merely result in tortuosity.

In making forty-one unselected post-mortem examinations of the basilar artery with due regard to arteriosclerotic changes, the length and width of the arteries, and the age of the patient, we have found the average length to be 34.4 mm, measured from the conjunction of the two vertebral arteries to the division into the posterior cerebral arteries. It is clear that it is not only the degree of the arteriosclerosis that decides the length and the width of the arteries, even if the longest and most winding vessels are usually the sites of the most advanced arteriosclerosis. Thus, for example, an 82-year-old patient was found to have a basilar artery that measured only 25 mm. In one case a basilar artery showing advanced arteriosclerosis had a length of 55 mm without deforming the third ventricle; the length was compensated by considerable tortuosity in the frontal plane, and the bifurcation was situated 1—2 cm laterally to the third ventricle. The topography resembles DANDY's cases.

It is thus evident that the description that we have given of the deformation of the third ventricle does not always occur in every case of an ectatic basilar artery, and further, that a high degree of arteriosclerotic changes can take place without the artery being elongated. In addition the autopsy material shows that considerable individual

variations exist as regards the length of the basilar artery. Out of fifteen basilar arteries, without, or with only very slight, arteriosclerosis, the shortest had a length of 27 mm and the longest a length of 39 mm. This latter vessel, which lay in the midline, did not deform the third ventricle. In all forty-one cases, with the exception of one (an anomaly as regards the basilar artery), the site of confluence of the two vertebral arteries was constantly situated close beside the furrow between the medulla oblongata and the posterior boundary of the pons. Only a variation of 1—2 mm was noted.

It must thus be clear that the basilar artery in different cases projects up into the cisterna pontis or interpeduncularis to varying degrees. The position of the bifurcation does not depend only upon the absolute length of the vessel but also upon its degree of tortuosity. This sometimes brings the position of the bifurcation to the side of, or behind, the nearest part of the third ventricle so that the latter does not become deformed. In certain cases in which the basilar bifurcation has an asymmetric position, the ventricle may be deformed by one or both posterior cerebral arteries.

Our investigations show: (1) That all roentgenologically examined patients with a long basilar artery deforming the third ventricle have been found to have high blood-pressures (200—240 mm Hg) and to be between fifty and sixty years of age. (2) A long basilar artery may deform the third ventricle so that a tumour in the hypothalamus, pons or basal cisternae, or an aneurysm in the basilar bifurcation is simulated. (3) Vertebral angiography is then necessary to provide a complete roentgenologic investigation. (4) An ectatic basilar artery only brings about a deformation of the third ventricle under certain conditions. (5) Any parallelism between a macroscopically observable degree of arteriosclerosi and the size of the basilar artery does not exist. (6) Purely individua variations in the length of the basilar artery are hardly enough to explain the size of the basilar arteries that deform the third ventricle. (7) Pathologico-anatomic investigations so far carried out support the assumption that a disturbance of the elastic substance in the walls of the arteries in connection with high blood-pressure, are the most important factors in bringing about extreme elongation and widening.

SUMMARY

The relation between the floor of the third ventricle and the basilar artery has been studied both roentgenologically and at autopsy. Five cases with a basilar impression in the floor of the ventricle are described. From clinical, roentgenologic, and pathologic-anatomic observations the authors have found that the deformation of the third ventricle caused by the basilar artery only occurs when the latter is enlarged. It is considered likely that this enlargement is principally caused by damage to the elastic tissue in the vessel, combined with high blood-pressure.

ZUSAMMENFASSUNG

Die Beziehungen zwischen dem Boden des 3. Ventrikels und der A. basilaris sind röntgenologisch und bei der Sektion studiert worden. Fünf Fälle mit einer basilaren Impression im Ventrikelboden werden beschrieben. Auf Grund von klinischen, röntgenologischen un pathologisch-anatomischen Beobachtungen haben die Verf. gefunden, dass eine Deformierung des 3. Ventrikels durch die A. basilaris nur dann auftritt, wenn die Letztere vergrössert ist. Man ist auch der Ansicht, dass eine derartige Vergrösserung hauptsächlich durch Schädigung der elastischen Gewebe der Gefässe in Kombination mit hohem Blutdruck entsteht.

RÉSUMÉ

Les auteurs ont étudié les rapports du plancher du troisième ventricule avec l'artère basilaire radiologiquement et à l'autopsie. Ils décrivent cinq cas de saillie de l'artère basilaire dans le plancher du ventricule. D'observations cliniques, radiologiques et anatomo-pathologiques les auteurs ont déduit que la déformation du troisième ventricule par l'artère basilaire ne se produit que quand celle-ci est augmentée de volume. Ils tiennent pour vraisemblable que cette augmentation de volume est surtout due à une lésion du tissu élastique du vaisseau, combinée à une hypertension artérielle.

REFERENCES

DABELOW, A.: Über Korrelationen in der phylogenet. Entwicklung der Schädelform. Gegenbaurs Morph. Jb 67 (1931), 84.

DANDY, W. E.: Intracranial arterial aneurysms. Comstock Publishing Comp. Inc., New York 1945.

DAVIDOFF, L. M. and DYKE, C. G.: The normal encephalogram. Lea and Febiger, Philadelphia 1951.

DAVIDOFF, L. M. and EPSTEIN, B. S.: The abnormal encephalogram. Lea and Febiger, Philadelphia 1950.

EPSTEIN, B. S.: A pneumoencephalographic study of the normal third and fourth cerebral ventricles and aqueduct of Sylvius. Am. J. Roentgenol. 63 (1950), 204.

GLYNN, L. E.: Medial defects in the circle of Willis and their relation to aneurysm formation. J. Path. & Bact. 51 (1940), 213.

HEIDRICH, L.: Die Encephalographie und Ventrikulographie. Ergebn. Chir. u. Orth. 20 (1927), 156.

LINDGREN, E.: A pneumographic study of the temporal horn. Acta radiol. Suppl. 69 (1948).

— Some aspects on the technique of encephalography. Acta radiol. 31 (1949), 161.

— Percutaneous angiography of the vertebral artery. Acta radiol. 33 (1950), 389.

— Air studies of the skull. Modern Trends in Diagnostic Radiology, Chapter XIX, p. 291. Butterworth & Co., London 1953.

LYSHOLM, E., EBENIUS, B. and SAHLSTEDT, H.: Das Ventrikulogramm, I. Teil. Acta radiol. Suppl. 24 (1935).

PALMGREN, Å.: Über Enzephalographie bei Kindern. Acta paediat. 25 (1939), 227.

RADNER, S.: Vertebral angiography by catheterization. Acta radiol. Suppl. 87 (1951).

SCHIERSMANN, O.: Einführung in die Enzephalographie. Georg Thieme, Stuttgart 1952.

SJÖGREN, S. E.: Percutaneous vertebral angiography. Acta radiol. 40 (1953), 113.

SUTTON, D.: The radiological assessment of the normal aqueduct and 4th ventricle. Brit. J. Radiol. 23 (1950), 208.

TWINING, E. W.: Posture in radiography of skull. Proc. Roy. Soc. Med. 27 (1934), 591.

— Radiology of the third and fourth ventricles. Brit. J. Radiol. 12 (1939), 385 and 569.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. OLLE OLSSON)
OF THE UNIVERSITY CLINICS OF LUND, SWEDEN

THE CERVICAL SPINAL CANAL IN INTRASPINAL EXPANSIVE PROCESSES

by

Erik Boijsen

Tumours in the spinal canal are capable of causing pressure atrophy with subsequent widening of the canal. These pressure changes are late signs but appear earlier in the growing skeleton in which the changes are also more pronounced (OLLE OLSSON, 1948).

The widening of the spinal canal has been described roentgenologically as an increased interpedicular distance. CAMP, ADSON & SHUGRUE (1933) and ELSBERG & DYKE (1934) were the first to stress the importance of directing careful attention to the pedicles in all cases in which a spinal tumour might be expected. ELSBERG & DYKE measured the interpedicular distances and gave a diagram of the normal values for different levels of the spine. They reported that it was often not possible to measure the interpedicular distances of the three or four uppermost cervical vertebrae. By means of tomography, however, these distances may be gauged, but, as will be apparent later, the results are of little value. LINDGREN (1937) pointed out that attention should be given to the sagittal diameter of the spinal canal in the cervical section of the spine. But only in one of his 15 patients with a cervical spinal tumour was he able to demonstrate a widening of the canal in a sagittal direction.

Author's Investigations

Lead plates were placed over the base of one of the pedicles of the fourth cervical vertebra as well as over the ventral part of the lamina (Fig. 1).

The pedicle is directed obliquely towards the dorsal surface of the

Submitted for publication, February 1, 1954.

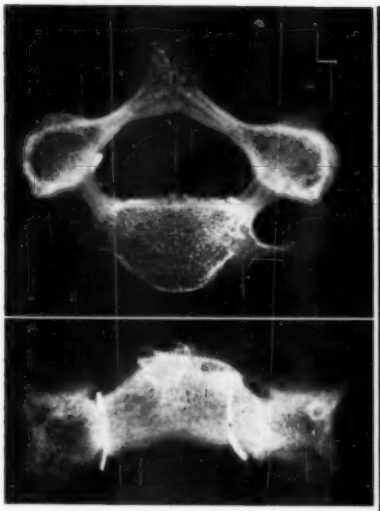


Fig. 1. C IV: axial and frontal view with lead plates on a lamina and a pedicular base.

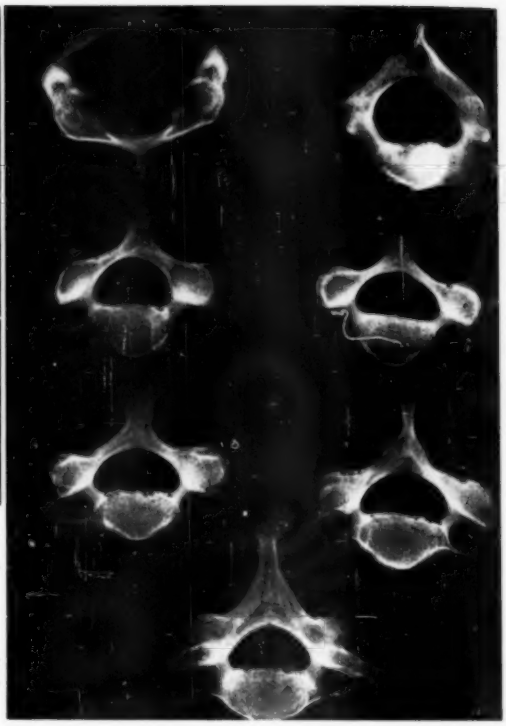


Fig. 2. C I—C VII: axial view. The frontal diameter is larger than the sagittal throughout.

vertebral body, its base lying medial to what is usually called the pedicle in frontal views. The so-called interpedicular distance in the cervical spine is thus not the distance between the pedicular bases, but the distance between the ventralmost parts of the laminae. This distance represents the greatest diameter of the spinal canal in this region, while the distance from the middle of the dorsal surface of the vertebral body to the union of the arches dorsally is the smallest diameter. This applies to all cervical vertebrae (Fig. 2). In the thoracic and in the lumbar section, however, the frontal diameter is just as large as the sagittal.

Similar to a long bone, the pedicle has a thick compacta, while the vertebral body is built like a spongy bone and has only a thin cortex. The pedicle should therefore be more resistant to pressure atrophy. The site of pressure atrophy will, of course, vary with the site of the tumour in the spinal canal. If the tumour is adjacent to the pedicle, this part of the vertebra will be affected first. If the tumour is intramedullary

or in the neighbourhood of the midline, the spinal canal will be initially affected where its diameter is smallest, *i. e.* in the cervical region, the sagittal diameter will be the first to show any changes.

The changes to be expected in the presence of expansive tumours of the cervical spinal canal are as follows:

1) *Excavation of the dorsal surface of the vertebral body*, deepest in the middle and becoming shallower cranially and caudally because of the buffering effect of the intervertebral disks. A cupping of the dorsal surface is also seen in osteoporosis and cervical spondylosis and must not be confused with excavation from pressure atrophy (LINDGREN, 1937).

2) *Erosion of the dorsal part of the laminae.* In lateral views this is seen as a decrease in the length of the spinous processes. As the normal range of variations of this length is wide, measurement of the spinous processes does not permit any conclusions as to the presence of a pathologic condition.

3) *Pressure atrophy in the other parts of the ring.*

Fig. 3. Lateral view of the normal cervical spine with the sagittal diameter outlined.

Widt of Cervical Spinal Canal

The normal range of variation in the sagittal diameter of the cervical part of the spinal canal is wide. Not until the limits of this range have been established is knowledge of the width of the canal of diagnostic value. For this purpose the cervical spines of 200 normal individuals (100 males, 100 females) were studied. The diameter, as seen in lateral views (Fig. 3), was measured from the middle of the dorsal surface of the vertebral body to the nearest point on the spinal process, with the exception of the atlas, in which the measurement was taken from the posterior surface of the axis at the level of the axis joint to the union of the arches dorsally.

The results are given graphically (Diagram 1). The sagittal diameter was greatest at the atlas, decreased caudally and was practically uniform

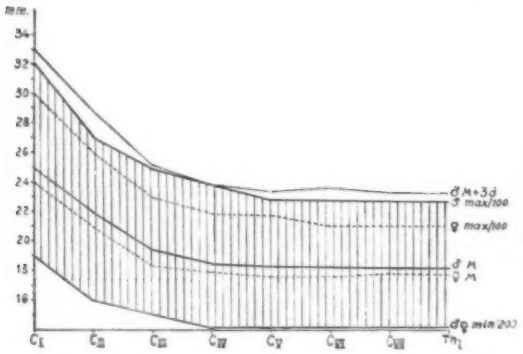


Diagram 1. Normal variations in the sagittal diameters recorded in 100 males and 100 females. M. = Arithmetic mean; max/100 = the largest diameters measured in either sex; min/200 = the smallest diameters measured in entire series.

from C V to C VII. As expected, the diameter was a few millimetres less in females.

The range of variation was considerable. This was due partly to the variation in the examination technique and partly to variation in body build (Table 1), but mainly to the normal variation in the cervical part of the spine. With a uniform examination technique — preferably with a focus-film distance of 1.5 m and with the cassette and grid against the shoulder this range of variation can be diminished by a few millimetres.

Table 1

Variation of the sagittal diameter with the focus—film (F—F) and object—film (O—F) distances

	F—F distance		Difference between 1 and 1.5 m F—F distance
	1 m	1.5 m	
Shoulder breadth 40 cm (O—F distance 20 cm)...	18.8 mm	17.3 mm	1.5 mm
Shoulder breadth 50 cm (O—F distance 25 cm)...	20.0 mm	18.0 mm	2.0 mm
Effect of 5 cm difference in O—F distance	1.2 mm	0.7 mm	

The sagittal diameter of the spinal canal was said to be 15 mm.

It is apparent from Diagram 1 that a deviation by $+ 3\ \sigma$ from the arithmetic mean for men approaches the upper limits recorded. If the distance recorded exceeds this upper limit an intraspinal expanding lesion must be considered.

The diagram shows that considerable pressure atrophy is necessary for producing roentgenographic changes, especially if the original sagittal diameter lies near the lower limit of the normal range. In such a case any such widening would have to exceed 10 mm before it could be

regarded as a sign of a tumour. This, provided that the tumour involves the entire cervical part of the spinal canal (cf. Case 6).

This is, however, not the case if the tumour is localized to the level of one or two of the cervical vertebrae. Then the sagittal diameters of the individual vertebrae involved must be compared with those of the neighbouring vertebrae. These variations were therefore studied in the 200 controls; the results are given in Table 2.

Table 2

Range of variation (in mm) in the sagittal diameter of neighbouring cervical vertebrae.

$$C^{I} \begin{matrix} < 2 \\ 9 \\ > \end{matrix} C_{II}$$

$$C^{II} \begin{matrix} < 1 \\ 8 \\ > \end{matrix} C_{III}$$

$$C_{III} \begin{matrix} < 1 \\ 5 \\ > \end{matrix} C_{IV}$$

$$C_{IV} \begin{matrix} < 2 \\ 2 \\ > \end{matrix} C_{V}$$

$$C_{V} \begin{matrix} < 2 \\ 2 \\ > \end{matrix} C_{VI}$$

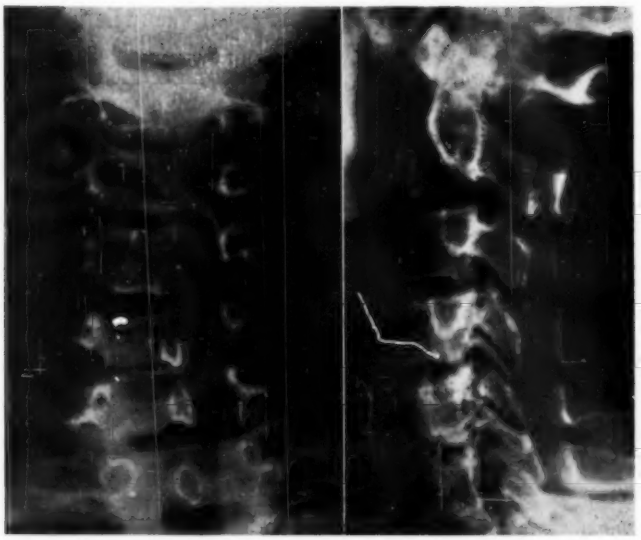
$$C^{VI} \begin{matrix} < 4 \\ 3 \\ > \end{matrix} C_{VII}$$

Should the diameter at C III, for example, be more than 6 mm greater than at C IV or 2 mm more than that at C II a tumour may be assumed. In such cases the diameter need not exceed the upper limits given in the diagram for the establishment of a diagnosis. In these cases the curve shows a pathologic peak.

In 30 of the 200 cases the diameter could also be measured at Th I. The diameter was regularly found to be the same as at C VII.

Diagnostic Significance of the Sagittal Diameter in the Cervical Part of the Spine

During the years 1947 to 1951, 13 patients in all were operated on (LUNDBERG) at the Neurosurgical Department, Lund, for primary, expansive processes of the cervical part of the spinal canal. Of these, 12 had been examined in the Roentgen Department and the expansive process diagnosed preoperatively by skeletal roentgenography and oxygen myelography. One case (a neurinoma) was diagnosed with lipiodol at another hospital. Of these tumours, 8 were intramedullary and 5 extramedullary. Only those cases with roentgenographically demonstrable skeletal changes are described below.



a. b.

Fig. 4. Case 1. a) A-P view. Pathologically wide frontal diameter. b) Lateral view. Distinctly increased sagittal diameter from C III to C VII.

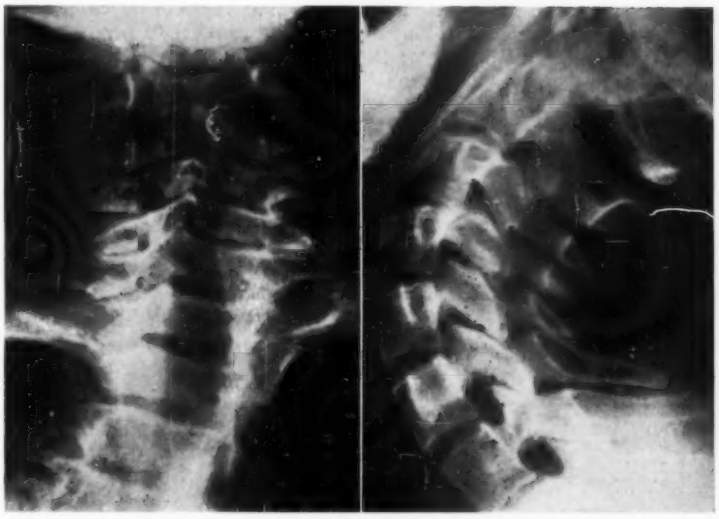
Case 1. (U. K. Vert. 730 d/50. Figs. 4 a and b). For two-and-a-half years the patient, a man aged 20, had had increasing contractures as well as weakness and fasciculation of the left hand. *Roentgen examination* of the cervical spine showed pathologically increased interpedicular distances from C IV to Th. I. The sagittal diameter was increased from C III to C VII (Diagram 2) and was largest at C IV—C VI where shallow excavation of the dorsal surface of the vertebral bodies was observed.

Operation. Laminectomy C I—C VI. The dural sac was distinctly widened and the extradural space completely obliterated. The arches of C IV—C VI were definitely eroded. The spinal cord was swollen because of syringomyelia, which exploration showed to extend from the foramen magnum down to the level of C VI. No tumour could be demonstrated. The dura was adherent to the upper part of the medulla and the cerebellar tonsils. No free posterior cistern was seen and the tonsils were lower than usual.

Diagnosis. Syringomyelia C I—C VI + Arnold-Chiari malformation.

Case 2. (L. K. Vert. 222 d/51. Figs. 5 a and b). A man, aged 23, who had pronounced scoliosis since childhood. He reported slowly increasing weakness of the right arm and leg during the previous two years. The interpedicular distances were slightly greater than normal, but in view of marked cervical lordosis this finding was of but little value and provided no conclusive information (a-p view). Vertebral bodies C II—C V showed slight excavation and the sagittal diameters of C II to C VI (Diagram 2) were increased.

Operation. Laminectomy C I—C VII. The extradural space was obliterated and the spinal canal wide in the section exposed. The medulla of the entire cervical spine



a. b.

Fig. 5. Case 2. a) A-P view. Scoliosis makes measurement of the frontal diameter difficult, but it appears to be within normal limits. b) Lateral view. Distinctly increased sagittal diameter.

was markedly thickened by an intramedullary cyst. A biopsy specimen from the wall showed glious tissue, poor in cells.

Diagnosis. Syringomyelia C I—C VII.

The remarkable feature about these two cases was that the expanding lesion, syringomyelia, had produced a roentgenographically demonstrable widening of the spinal canal. This finding, as far as I have been able to ascertain, has not been reported in association with isolated syringomyelia. On the other hand, FRIEDL (1946) reported roentgenographic widening of the cervical section of the spinal canal in congenital syringomyelia from a glioma.

As the hydromyelia in the two cases described above showed such marked expansiveness, it is possible that it was combined with a glioma further down in the medulla. ANTONI (1936) described a large number of cases with intramedullary glioma in combination with syringomyelia. BITTORF's case is of special interest. The patient had syringomyelia in the medulla of the cervical spine and in the upper thoracic region was a small glioma. A similar case was described by DOWMAN & SMITH (1929), who suggested that in all cases of syringomyelia a search should be made for a tumour. Case 2 showed the typical marginal gliosis seen in combination with glioma. According to KERNOHAN (1934), anything up to 80 per cent of all gliomas are associated with cavitation of the medulla.

Regarding Case 1, it is more likely that the widening of the canal was due to syringomyelia associated with Arnold-Chiari malformation. According to LICHTENSTEIN (1943) syringomyelia appears in different ways in Arnold-Chiari malformation. It may be due to an ischemic necrosis from constriction at the atlas by suppression of the tonsils (the cervical medulla receives its blood supply from the cranium) (this form can never be expansive, but only cause local destruction of the cord) or by pressure on the fourth ventricle by the plexus chorioideus down past the foramen magnum. This results in a poor communication between the distal end of the fourth ventricle and the posterior cistern. Excess liquor flows down into the central canal, which is still open in young people, and hydromyelia arises. This form is distinctly expansive and when the cavity becomes large enough, it can probably affect the spinal canal. The common form of syringomyelia, *i. e.* the form of unknown origin, is certainly progressive but it is doubtful whether it can cause such marked expansion as in these two cases.

The skeletal changes seen in Arnold-Chiari malformation have been described by many authors such as GUSTAFSON & OLDBERG (1940), LIST (1941), ADAMS et al. (1941), EPSTEIN (1948), GARDNER & GOODALL (1950). These changes have also been present in combination with spina bifida, deformations of the type KLIPPEL-FEIL and platybasia. Sometimes it has been possible in a few single cases to establish the diagnosis with lipiodol, when the tonsils appeared as defects in the contrast filling and the posterior cistern was absent (ADAMS et al. 1941, EPSTEIN, LIST, MALIS et al. 1951). Coexistent hydromyelia is common, but a search of the literature failed to reveal any report of a case with widened spinal canal. In LIST's Case 4 the patient had Arnold-Chiari malformation and post-mortem examination revealed hydromyelia in the lower cervical and upper thoracic medulla. The accompanying roentgenographic reproductions show a definite increase in the sagittal diameter of the spinal

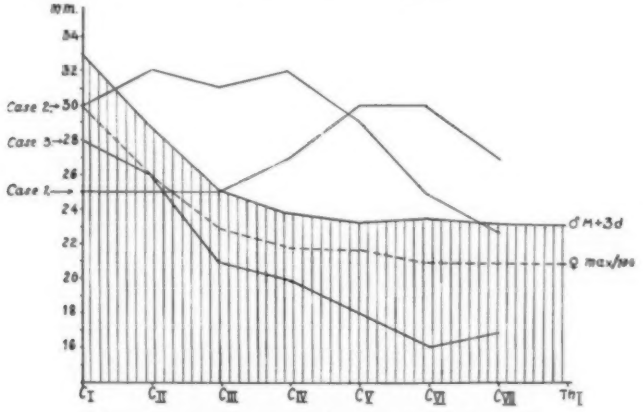
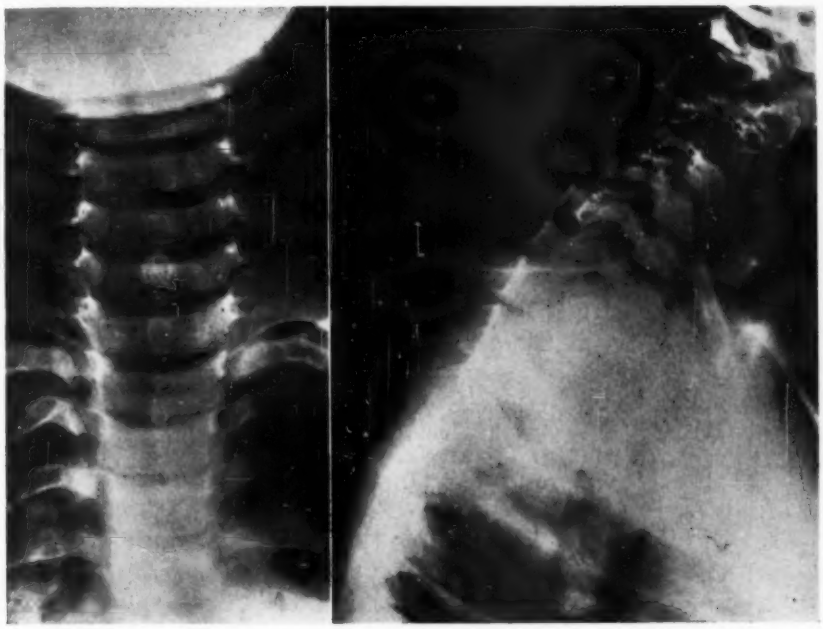


Diagram 2. Case 1. Syringomyelia C I—C VI.
» 2. » C I—C VII.
» 3. » C I—C IV.



a. b.

Fig. 6. Case 4. a) A-P view. Pathologically increased frontal diameter C IV—Th IV. b) Lateral view. Increased sagittal diameter C IV—Th IV.

canal in its lower cervical section, a finding which was, however, not mentioned by LIST.

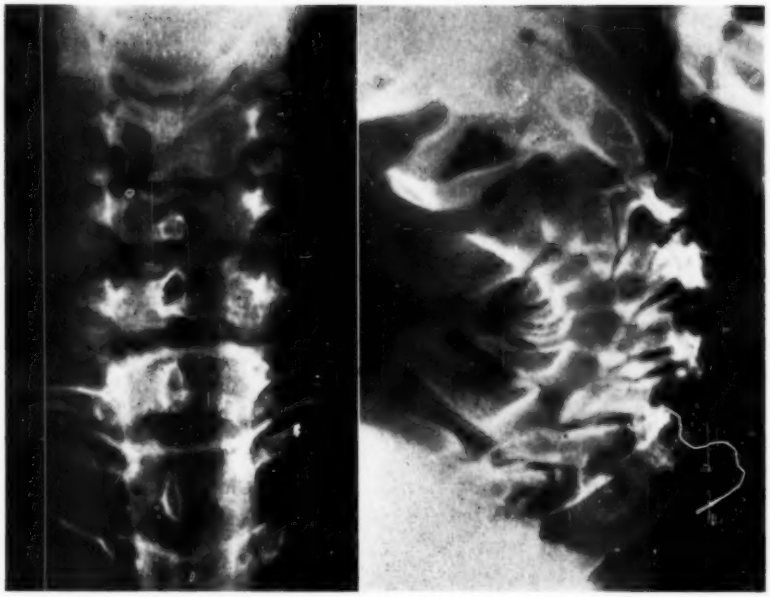
An observation of interest in these two cases is that only a slight proportion of the expansion in a sagittal direction was ascribable to the excavation of the dorsal surfaces of the vertebral bodies. Pressure atrophy had affected mainly the laminae. Despite the shortness of the history, it is possible that in these two cases syringomyelia dated back to childhood and had widened the spinal canal before its final ossification.

Syringomyelia was also seen in association with Arnold-Chiari malformation in one of the other cases (Diagram 2).

Case 3. (A. O. Vert. 448 def./47). A woman, aged 62, who had for one year had increasing loss of heat sensation of the hands.

Roentgen examination of the cervical spine showed normal interpedicular distances and sagittal diameters. At C II, however, the diameter bordered the upper normal limit for women (Diagram 2).

Operation. Laminectomy C I—C V. In the region explored the dura was distended and the extradural fat diminished. The records contained no note as to whether the



a. b.

Fig. 7. Case 5. a) A-P view. The frontal diameter is increased but owing to marked lordosis it is difficult to say with certainty whether the increase is pathologic. b) Lateral view. The sagittal diameter increased from C I to Th I.

arches were eroded. The cerebellar tonsils extended down to the margin of the atlas and the posterior cistern was missing. The medulla was thickened by syringomyelia extending from C I to C IV.

Diagnosis. Arnold-Chiari malformation with syringomyelia C I—C IV.

Glioma was seen in as many as five of the present cases. In two of these the spinal canal was definitely widened, mostly in a sagittal direction.

Case 4. (D. J. Vert. 684 var/47. Figs. 6 a and b). The patient was a boy, aged 6, whose head had been fixed in forward flexion for three years. Three months before admission attempts were made to correct the position under anaesthesia, it being thought that it was a sequel of poliomyelitis. In connection with the attempted correction signs of cerebral compression and paresis of the arms appeared.

Roentgen examination of the cervical and thoracic spine showed increased interpedicular distances of C IV—Th IV and an increased sagittal diameter in the same region.

Operation. Laminectomy Th II—Th III. The arches were thin and the extradural space was obliterated. Underneath the dura was a tumour which was as thick as a thumb

and proved to be a malignant astrocytoma. No attempts were made to extirpate the mass so that nothing further can be said about its size.

Diagnosis. Astrocytoma probably extending from C IV to Th IV.

Case 5. (I. R. Cr. c. 261/50. Figs. 7 a and b). A woman, aged 21. For the previous 6 years she had had paresis of the left arm, and for the previous three years, of both legs and the right arm.

Roentgen examination of the cervical spine showed pronounced cervical lordosis with increased sagittal diameter of the spinal canal from C I to Th I (Diagram 3). The interpedicular distances admittedly exceeded the upper limit of the ordinary range, but because of the pronounced cervical lordosis they could not be classed as definitely abnormal. On the other hand the pedicles of Th I—Th IV were eroded.

Operation. Laminectomy C I—Th IV. The medulla was thickened from C I to Th IV, where it began to taper. The dura was distended at the level of C IV—C V. Infiltrating growth present.

Diagnosis. Astrocytoma C I—Th IV.

In both of these cases of malignant glioma, the tumour grew slowly and therefore produced skeletal changes. In Case 4 ossification was not yet complete. In Case 5 the symptoms appeared at the age of 15. The tumour might have been present before ossification of the cartilage of the arches. In this case, the vertebral bodies which were of ordinary size, showed no excavation. On the other hand the spinous processes were small, especially those of C III to C IV. The relative smallness of the vertebral bodies (despite ordinary body build) in relation to the sagittal diameters was striking.

The significance of studying the sagittal diameter is illustrated by Case 4 in which the upper border of the tumour could not be recognized in the frontal view but was distinctly seen in the lateral view.

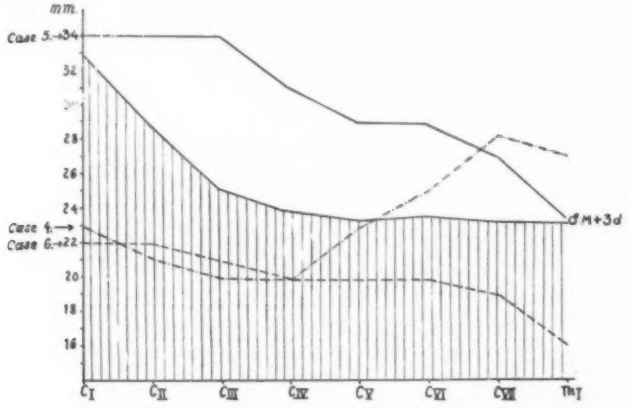


Diagram 3. Case 4. Astrocytoma C IV—Th IV.
» 5. » C I—Th IV.
» 6. Astroblastoma C I—Th II.

Another case of glioma in the cervical spinal cord was of interest although it was not possible to demonstrate any widening of the spinal canal with certainty.

Case 6. (E. H. Myel. 41 s/49). A man, aged 41, had for 4 years "pins and needles" in the hands and decreased reaction to heat and cold.

Roentgen examination showed normal interpedicular distances and normal width of the spinal canal in the sagittal plane.

Operation. Laminectomy C I—Th II. The dural sac was definitely dilated, the extradural space being obliterated and the arches within the entire cervical spine eroded. There was an encapsulated tumour the thickness of a small finger in the medulla.

Diagnosis. Astroblastoma C I—Th II.

In Case 6, then, the sagittal diameter of the entire cervical spine was normal throughout (Diagram 3). However, a slight difference between the diameter at the atlas-axis level and in the other vertebrae, was quite definite. No excavation of the vertebral bodies was observed. In this case the curve was very flat but such curves are also seen in normals. In view of the observations made at operation, it must be assumed that the original sagittal diameter at the level of vertebral bodies C III—C VII was some millimetres less. This was also confirmed by the fact that at Th I the sagittal diameter was 3 mm less than at C VII, a difference never seen in normals. In the two uppermost cervical vertebrae the diameter is normally so large that skeletal changes do not appear until late.

To summarize, of 5 histologically verified cases of glioma of the cervical spinal cord, 2 showed a distinct increase in the sagittal diameter of the cervical spinal canal and in a further case there was reason to suspect a tumour. In the remaining 2 cases of glioma of the cervical cord both at the level of C I—C II, no skeletal changes could be demonstrated. In these 2 cases the patients, aged 48 and 46 had had symptoms for 4 and 2 years, respectively.

Of the 4 cases of neurinoma, skeletal changes were demonstrated in 3. In 2 of them the only change was a widening of the foramina intervertebralia. In the third the sagittal diameter of the spinal canal at the level of the tumour was abnormally large.

Case 7. (O. P. Vert. 109 def/51). A man, aged 59, who for 1 year had had back pain and numbness in the feet. Examination of the skeleton revealed no signs of a tumour but myelography showed an expansive process in the region of C VI to Th II.

Operation. Dorsal to the medulla was an intradural tumour the thickness of a small finger, 4 cm long, and extending from C VI to Th II.

Diagnosis. Neurinoma C VI—Th II.

On re-examination of the skeletal films and measurement of the sagittal diameters it was observed that at the level of C VII and Th I

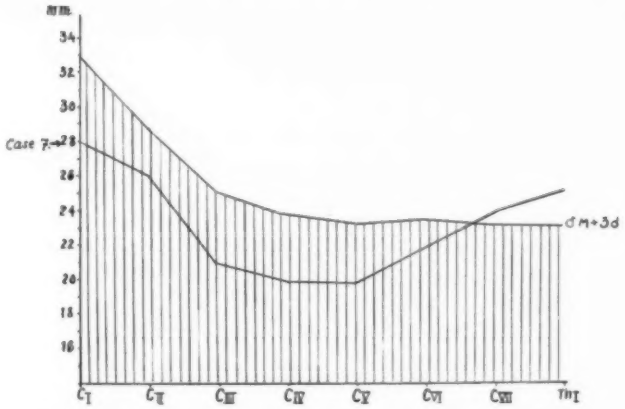


Diagram 4. Case 7. Intradural neurinoma C VI—Th II.

it exceeded the normal upper limit (Diagram 4). No signs of destruction were seen and the interpedicular distances were normal. Thus, if the sagittal diameters had been measured routinely in all cases of suspected tumour, a diagnosis of tumour would have been possible in this case.

A fourth neurinoma and an extradural meningeoma produced no demonstrable skeletal changes.

Discussion

Of our 13 cases of intraspinal primary expansive processes of the cervical section, skeletal changes were seen in 7. This is an unusually high figure, although high figures are on record but not for the cervical spine only. LINDGREN (1937) gave a percentage of 29 out of his 67 cases with primary expansive intraspinal growth. Nine of them were intramedullary (none localized to the cervical section) but in only 1 case was the spinal canal widened. CAMP found skeletal changes in as many as 50 per cent in the presence of extradural tumours, but he claimed that the effect on the skeleton was rare in intramedullary processes because he himself had never seen such a case.

Nevertheless, the high frequency in the present series is due mainly to the relatively large number of intramedullary processes (8 cases). According to KERNOHAN (1932), the average duration of intramedullary tumours is 4.9 years while for extramedullary tumours it is 2 years less. Gliomas have been described which have grown for 30 years (ANTONI 1936). With such a long duration it is understandable that the spinal canal can be affected. FRIEDL (1946) is of the opinion that in the cer-

vical section only congenital slowly growing gliomas or syringomyelia secondary to gliomas can widen the spinal canal.

A second important cause of the high frequency of skeletal changes in the present series was that all of the intramedullary tumours with a widening of the spinal canal were seen in young people. One may therefore presume that the tumour was present before ossification of the growth centres, which, according to RUCKENSTEINER (1931), normally takes place over a period of almost 8 years.

A third factor is the fact that the sagittal diameter was measured. Of the 7 cases with skeletal changes, 5 showed increased sagittal diameter, while only 2 showed distinctly pathologic interpedicular distances and then in combination with sagittal widening of the spinal canal. In no case, was an increased interpedicular distance the only change observed.

In one of the cases excavation of the dorsal surface of the vertebral bodies was pronounced, while in 2 it was only slight and therefore readily missed. In 2 cases (Cases 5 and 7) no excavation of the dorsal surface was seen but the sagittal diameter was nevertheless definitely pathologic.

SUMMARY

The measurement of the sagittal diameter of the cervical spinal canal based upon 200 normal subjects is described and the diagnostic significance of the procedure pointed out. Seven case reports out of a material of 13 cases are presented and attention drawn to the high frequency of skeletal changes in the presence of cervical intraspinal expansive processes.

ZUSAMMENFASSUNG

Die Dimensionen des Sagittaldurchmessers des cervicalen Spinalkanales, die sich auf Messungen an 200 gesunden Personen gründen, werden beschrieben. Aus einem Material von 13 Fällen werden 7 Fälle geschildert und die Aufmerksamkeit wird auf die Frequenz von Skelettveränderungen beim Vorhandensein von cervicalen intraspinalen expansiven Prozessen gerichtet.

RÉSUMÉ

L'auteur rend compte de la mesure du diamètre sagittal du canal rachidien cervical faite chez 200 sujets normaux et souligne l'importance diagnostique de cette mesure. Il présente les observations de sept cas sur un matériel de treize cas et attire l'attention sur la fréquence élevée des modifications osseuses en présence de tumeurs intrarachidiennes cervicales.

REFERENCES

ADAMS, R. D., SCHATZKI, R. and SCOVILLE, W. B.: Arnold-Chiari malformation; diagnosis, demonstration by intraspinal lipiodol and successful surgical treatment. New England J. Med. 225 (1941), 125.

ANTONI, N.: Handbuch der Neurologie. Bd. XIV. J. Springer Verlag, Leipzig 1936.

BERKWITZ, N.: Extensive longitudinal cavitation of the spinal cord associated with a circumscribed intramedullary tumour. Arch. Neurol. & Psychiat. 32 (1934), 569.

BITTORF, A.: Beiträge zur pathologischen Anatomie der Gehirn- und Rückenmarksgeschwülste. Beitr. z. path. Anat. u. z. allg. Path. 35 (1904), 169.

CAMP, J. D.: The significance of osseous changes in the roentgenographic diagnosis of tumours of the spinal cord and associated soft tissues. Radiology 22 (1934), 295.

CAMP, J. D., ADSON, A. W. and SHUGRUE, J. J.: Roentgenographic findings associated with tumours of the spinal column, spinal cord and associated tissues. Am. J. Cancer 17 (1933), 348.

DOWMAN, C. E. and SMITH, W. A.: Intramedullary cyst of the spinal cord associated with a circumscribed intramedullary tumor. Arch. Neurol. & Psychiat. 21 (1929), 583.

ELSBERG, C. A. and DYKE, C. G.: The diagnosis and localization of tumors of the spinal cord by means of measurements made on the X-ray films of the vertebrae, and the correlation of clinical and X-ray findings. Bull. Neurol. Inst. New York 3 (1934), 359.

ELSBERG, C. A.: Surgical Diseases of the Spinal Cord. P. Hoeber, New York 1944.

EPSTEIN, S. B.: Pantopaque myelography in the diagnosis of the Arnold-Chiari malformation without concomitant skeletal or central nervous system defects. Am. J. Roentgenol. 59 (1948), 359.

FRIEDL, E.: Erweiterung des Wirbelkanales bei Geschwülsten des Rückenmarkes, der Nervenwurzeln und der Rückenmarkshäute. Radiol. Clin. 15 (1946), 275.

GARDNER, J. and GOODALL, R.: The surgical treatment of Arnold-Chiari malformation in adults. An explanation of its mechanism and importance of encephalography in diagnosis. J. Neurosurg. 7 (1950), 199.

GUSTAFSON, W. A. and OLDBERG, E.: Neurologic significance of platybasia. Arch. Neurol. & Psychiat. 44 (1940), 1184.

INGRAHAM, F. D.: Intraspinal tumors in infancy and childhood. Am. J. Surg. 39 (1938), 342.

KERNOHAN, J. W.: Primary tumors of the spinal cord and intradural filum terminale. *In* PENFIELD: Cytology & Cellular Pathology of the Nervous System. Vol. III, p. 933. P. Hoeber, New York 1932.

— Personal communication to BERKWITZ, N.

LICHTENSTEIN, B. W.: Cervical syringomyelia and syringomyelia-like states associated with Arnold-Chiari deformity and platybasia. Arch. Neurol. & Psychiat. 49 (1943), 881.

LINDGREN, E.: Über Skelettveränderungen bei Rückenmarkstumoren. Nervenartz 10 (1937), 240.

LIST, C. F.: Neurologic syndromes accompanying developmental anomalies of the occipital bone, atlas and axis. Arch. Neurol. & Psychiat. 45 (1941), 577.

MALIS, L. I., COHEN, I. and GROSS, S. W.: Arnold-Chiari malformation. Arch. Surg. 63 (1951), 783.

OLSSON, O.: Roentgendiagnostic points of view on spinal tumors in children. Acta radiol. 29 (1948), 279.

RAUBER-KOPSCH: Lehrbuch und Atlas der Anatomie des Menschen Bd. I, p. 174. G. Thieme Verlag, Leipzig 1940.

RUCKENSTEINER, E.: Die normale Entwicklung des Knochensystems im Röntgenbild. G. Thieme Verlag, Leipzig 1931.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR: DOCTOR OLOV FR. HOLM),
LASARETTET, FALKÖPING, SWEDEN

FREE GAS IN THE FETAL VESSELS AS A ROENTGENOLOGIC SIGN OF INTRA-UTERINE FETAL DEATH

by

Olov Fr. Holm

The roentgen investigations aimed at demonstrating intra-uterine fetal death may be divided into two main groups: those indicating the absence of manifestations of life in the fetus, and those showing signs of maceration.

The first group includes the absence of continuous growth and the possibility of demonstrating in a series of roentgenograms taken with the mother lying in the same position that the fetus has not moved. This group also includes amniography, which is based on the principle that a living fetus drinks amniotic fluid. Thus, contrast medium injected into the amniotic sac may gradually be visualized in the gastro-intestinal canal of the fetus. This method is not risk-free with the present contrast solutions.

The value of the investigations aimed at showing fetal maceration depends upon the extent to which the condition has advanced.

Maceration is classified according to degree:

Grade I after 1 to 2 days;
Grade II after 4 to 5 days;
Grade III after approximately 12 days.

The roentgenologic signs of maceration may be divided into those in the head and those in the body. Among the signs in the head, SPALDING's sign is the most common and most important. This is caused by shrinkage

Submitted for publication, January 23, 1954.

of the head, with a decrease in volume, resulting in overlapping of the skull bones. BILLING demonstrated that similar roentgenograms may be obtained from a living fetus if there is a difference in level between the cranial bones. A projection with the beam direction parallel to the suture in question is therefore necessary. The other signs in the skull include a flattening of the convexity, severe asymmetry and, in some cases, enlargement with separation of the bones.

The most common signs of maceration in the body are due to a decrease in tonus and rigidity. Among these are severe curvature of the spine, marked lordosis in its caudal part, possible turning of the head of the fetus up to 180 degrees and a decrease in the skeletal calcium content. It is probable that the maceration group also includes a phenomenon of unexplained nature described by DEUEL. This consists of a narrow clear zone around the head of the fetus. It has been likened to a halo.

Fig. 1. Survey roentgenogram. Fetus in vertex presentation. A slight difference in level may be observed in the coronal suture, and a slight overlapping of the bones. Abundant gas in the abdominal aorta with gas also present in the liver region.

The occurrence of free gas in the fetal vessels may also, in all probability, be regarded as a sign of maceration. This is an unusual phenomenon. The writer has been able to find only five cases described in the literature. Two of these were reported by ROBERTS (1944), two by DAVIDSON (1949) and one by KETTUNEN (1952).

The following case may be added:

Case history: The patient was a woman, aged 29; gravida III. Since 1933 she had had diabetes and received 36 I. U. protamine zinc insulin. 1940: erythema nodosum, with subsequent joint symptoms. In 1950 she underwent operation for a benign tumour in the

Fig. 2. Oblique projection. Abundant gas may be seen in the aorta and common iliac arteries as well as in the liver region.

left breast. Radiotherapy was not administered. The first pregnancy terminated in premature delivery six weeks before the expected date. The baby, who died during the course of labour, weighed 1,700 grams. The second pregnancy terminated in abortion during the third month.

Third pregnancy: The reported date of the last menstruation was 10 February, 1953. Delivery was expected on 17 November, 1953. She had felt fetal movement since the middle of June. The patient had no symptoms during the entire pregnancy, but was referred to the Obstetric Department of Falköping Provincial Hospital because of sugar and albumin in the urine. She had had albuminuria since 8 October. At the time of admission on 10 October her general condition was unaffected, and she had no pain. Examination of the heart and lungs showed nothing pathologic. Temperature: 37.3° C, pulse 72, blood pressure 130/100. There was edema of the legs. The abdomen measured 87 cm, and the uterus extended up to 3 or 4 cm below the xiphoid process. The fetus was in a vertex presentation. The fetal heartbeat was heard: 140/minute.

Examination on 12 October showed vision and the retinas to be normal. The urine contained 0.1 per cent albumin. The Wasserman reaction was negative. The patient was blood group 0 and Rh +. She had never received a blood transfusion.

On 15 October no fetal sounds could be heard.

On 22 October again no fetal sounds could be heard.

Roentgen examination on that date showed a fetus in a vertex presentation. A slight displacement in level and a certain degree of overlapping of the bones of the skull were observed. Corresponding to the fetal abdominal aorta and common iliac arteries as well as in the fetal liver region abundant gas was visualized (Figs. 1 to 3). On the basis of the roentgen findings the diagnosis of intra-uterine fetal death was made.

At 7 a. m. on 23 October an unsuccessful attempt was made to rupture the amniotic sac. At 10 a. m. the same day prepartal treatment was initiated. At 11.30 p. m. a greatly macerated female child was delivered. The weight was 1,700 grams and the length 43 cm. The amniotic fluid was rust-coloured.

Roentgen examination of the fetus showed abundant gas in the heart and ascending aorta as well as in the liver region. In addition some smaller air bubbles were found in the head.

Autopsy of the fetus revealed grade III maceration. There was no contact between the bones of the skull, and the head was easily deformable. Small bubbles of air escaped on dissection of the heart and aorta under water.

Discussion

In maceration a shrinking occurs, a decrease in fetal volume. NEUWEILER stated that full-term living fetuses in his material had a mean weight of 3,344.8 grams, while the corresponding figure for full-term dead fetuses was 2,962 grams. In the present case the fetus weighed 1,700 grams, which is remarkably little in proportion to the length. Hemolysis appears in the blood primarily, and it becomes thin and dark brown. The hemoglobin then breaks down, with precipitation of bilirubin crystals. No putrefaction occurs in a closed amniotic sac. This can take place only when the membranes have ruptured and bacteria have entered from the vagina. A dead fetus may even dry up, and this may lead to complete mummification. The writer has been unable to find any reports in the pathologic literature that gas is formed in the fetal vessels. There is no explanation covering the fact that it can occur at all. DAVIDSON considered that the gas could arise through some unexplained decomposition of the blood. In the case reported by KETTUNEN, the mother was Rh negative while the father and earlier children were Rh positive. Accordingly, the mother was Rh immunized, and KETTUNEN was of the opinion that this was significant in the origin of the gas. In the writer's case the mother was Rh positive, and thus the Rh factor can have no essential significance.

Fig. 3. Roentgenogram of the fetus after delivery. The greater part of the gas now lies within the heart and thoracic aorta. A few large and many small gas-filled vessels may be seen within the liver.

The following mechanism for the origin of the gas might be conceivable. When the hemoglobin breaks down, its specific oxygen-absorptive capacity is abolished. If this breakdown takes place very rapidly, it is possible that so much oxygen is liberated that it cannot physically be dissolved in the available, unmoving blood fluid, but is collected in the vessel as free gas. If this conception is correct, the gas should consist

principally of oxygen. It is also possible that this is supported by a certain vacuum effect caused by the force that produces shrinkage of the fetus, in which case the large arteries are probably the only cavities in the flaccid fetal body with sufficient rigidity in the walls for the vacuum effect to act upon. Probably this sign is not so unusual as hitherto considered.

SUMMARY

The roentgenologic signs of intra-uterine fetal death are discussed. A case is described in which this diagnosis was established through demonstration of gas in the arterial system of the fetus.

An explanation of the conceivable origin of the gas is presented.

ZUSAMMENFASSUNG

Die röntgenologischen Symptome des intrauterinen Foetustoden werden besprochen. Ein Fall wird beschrieben, in dem die Diagnose durch die Demonstration von Gasen innerhalb des arteriellen Systemes des Foetus sichergestellt wurde.

Eine Erklärung betreffs der Entstehung der Gase wird vorgebracht.

RÉSUMÉ

L'auteur étudie les signes radiologiques de la mort foetale intra-utérine. Il présente un cas où ce diagnostic fut établi par la mise en évidence de gaz dans le système artériel du foetus.

Il propose une explication de l'origine de ce gaz.

REFERENCES

Billing, L.: Über die Deutung des röntgenographischen Übereinanderschiebens der Schädelknochen des Fötus. Acta radiol. 22 (1941), 277.

Davidson, C. N.: Roentgen demonstration of fetal death (gas within the fetus) and uterine rupture. Am. J. Roentgenol. 62 (1949), 837.

Deuel, H.: Zur Röntgendiagnose des intrauterinen Fruchttodes. Schweiz. Med. Wchnschr. 77 (1947), 1003.

Kaufmann, E.: Spezielle Pathologische Anatomie. Siebente und achte Auflage. Walter de Guyter & Co., Berlin und Leipzig 1929.

Kettunen, K.: Fetal death diagnosed roentgenographically by the presence of gas in the fetal circulatory system. Acta radiol. 37 (1952), 81.

Neuweiler, B.: Der intrauterine Fruchttod. Gynaecologia 127 (1949), 367.

Roberts, J. B.: Gas in the fetal circulatory system as a sign of intrauterine fetal death. Am. J. Roentgenol. 51 (1944), 631.

Spalding, A. B.: Pathognomonic sign of intrauterine death. Surg. Gynec. & Obst. 34 (1922), 754.

Zuppinger, A.: *In* Lehrbuch der Röntgendiagnostik von Schinz, Baensch, Friedl und Uhlinger. Fünfte Auflage, p. 3719, Georg Thieme Verlag, Stuttgart 1952.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. OLLE OLSSON) AND THE INSTITUTE OF PATHOLOGY (DIRECTOR: PROF. C. G. AHLSTRÖM), UNIVERSITY OF LUND, SWEDEN

ON THE TOLERANCE OF THE RABBIT'S KIDNEY TO CONTRAST MEDIA IN RENAL ANGIOGRAPHY

A Roentgenologic and Histologic Investigation

by

Hans Idbohrn and *Nils Berg*

The increasing use of renal angiography calls for more accurate knowledge of the tolerance of the kidney to contrast media. There is both experimental and clinical evidence that the employment of the common contrast media in renal angiography imposes certain risks.

BACCAGLINI and BALLARIN (1940), who used OSELLADORE's (1937) technique (aortography by means of a catheter passed into the aorta via a branch of the femoral artery) studied the effect of hypertonic saline (30 per cent), sodium iodide (75 and 100 per cent), strontium iodide (85 per cent) and Uroselectan B on the kidney. They observed renal stasis and initial degeneration of the epithelial cells of the convoluted tubules. They expressed the view that the injury was due to physicochemical factors.

SCRUFARI and DALLA POZZA (1949) injected Joduron 30 % into the aorta and renal artery of rabbits. As early as 3—5 minutes changes were seen in the tubuli in the form of cloudy swelling of the epithelial cells. The glomeruli were ischaemic and showed scattered interstitial haemorrhages which increased in intensity for 2 days and then gradually disappeared. The authors stressed, however, that with kidneys already diseased the injection may cause transient azotaemia. It is difficult to assess the actual concentration of the radiopaque medium in the kidney in these experiments, because the blood supply to the kidney was not shut off during the injection.

HENLINE and MOORE (1936), who studied the side effects of aortography on dogs, reported 3 deaths from the toxic effect of 100 per cent

Submitted for publication, December 15, 1953.

sodium iodide. Clinical aortography using 80—100 per cent sodium iodide is known to have caused focal renal necrosis (DUCUING, PONS and ENJALBERT, 1949), and death from mesenteric thrombosis due to the injection (WAGNER and PRICE, 1950). According to SMITH, RUSH and EVANS (1951), the injection of organic iodide compounds into the mesenteric artery is not attended by undue risks.

LARSSON and PALMLÖV (1952) reported a case in which the contrast medium (30 ml Dijodon 70 %) was injected near the origin of the right renal artery which apparently received the entire amount. A temporary impairment of the urea clearance test was observed. They were, however, not able to demonstrate any other untoward effect of the injection.

We have seen a case in which translumbar aortography was performed at another hospital on account of papilloma of the renal pelvis of the left kidney. The right renal artery was punctured, and a selective filling was obtained of this vessel with a pronounced nephrographic effect in the right kidney. After puncture of the aorta proximal to the origin of the renal arteries a second injection was given. Left nephrectomy 3 days later was followed by anuria with increasing N.P.N., and despite dialysis treatment, the patient died 6 weeks after aortography. The right kidney was considerably enlarged and microscopic examination showed pronounced damage, mainly of the convoluted tubules. It seems probable that the function of the right kidney had been impaired by the aortographic examination and that renal insufficiency had been masked by the good function of the left kidney. Thus, no symptoms or signs of impaired renal function were noted until after operation.

From these cases and the increasing use of renal angiography it was thought justified to investigate the tolerance of the kidney to contrast media. Umbradil was chosen, because it is commonly used in renal angiography and was found by BROMAN and OLLE OLSSON (1948—49) to be the least injurious of a number of contrast media studied for side-effects in experimental cerebral angiography.

Authors' Investigations

Contrast media. Umbradil (Astra) was used in 35 and 17.5 per cent and Umbradil forte (Astra) in 50, 25 and 10 per cent concentrations. (Umbradil is the diethanolamine salt of 3 : 5 di-iodide-4-pyridone-N-acetic acid in 35 per cent concentration. Umbradil forte is the diethanolamine and diethylamine salt of the same compound in 50 per cent aqueous solution.)

Experimental animals. 109 rabbits weighing on the average 2 kg were used. A few of the animals were found to have internal lesions —especially of the liver — due to coccidiosis. These animals were, however, included in the analysis of the results provided that the tissue changes were slight and had not involved the kidneys. Three of the animals were excluded because of bilateral focal non-specific nephritis with associated small abscesses.

Technique. The following three types of experiment were used:

Laparotomy and injection of the contrast medium into the renal artery (Method I).

Laparotomy and injection of the contrast medium into the abdominal aorta (Method II).

Injection of the contrast medium into the exposed carotid artery without laparotomy (Method III).

The animals were anaesthetised with Nembutal (0.5 ml/kg bodyweight) plus ether, as required.

In Methods I and II the operative field was depilated and an incision made in the midline. The intestines were pushed aside and packed with sterile tampons moistened with warm (37° C) normal saline.

Method I. A segment of the renal artery was carefully dissected free and a curved pincette was passed underneath the vessel. The pincette was then lifted and the blood supply to the kidney thereby shut off. The completely obstructed renal artery was punctured with a fine cannula (0.5 mm external diameter) immediately distal to the pincette and 1.0 ml contrast medium (in 1 experiment 2.0 ml) was injected under steady pressure. The injection was continuous and spread over a predetermined period varying from 15 seconds to 4 minutes; usually, however, the injection time was limited to 15 seconds. The cannula and the pincette were then removed and the blood again flowed into the kidney. Bleeding from the punctured vessel was controlled by gentle application of a sterile tampon for a minute or so. The interval during which the blood supply to the kidney was shut off was noted.

This type of experiment was carried out on 24 animals. Umbradil forte was used (in 1 case Umbradil was employed). In 6 experiments contrast medium was injected into both renal arteries. (Table I.)

Table I

Survey of Material treated according to Method I and Method II

Conc. Umbradil	No. of animals	No. of injections	Interval between injection and post-mortem examination				
			5—18 minutes	1—3 hours	10—17 hours	18 hours—3 days	3—13 days
Method I (24 rabbits)							
50 %	23	28	9	7	6	4	2
35 %	1	2	2	—	—	—	—
Method II (65 rabbits)							
50 %	23	—	2	3	8	5	5
35 %	9	—	2	1	3	2	1
25 %	9	—	2	2	2	3	—
17.5 %	15	—	4	3	2	4	2
10 %	9	—	—	—	5	4	—

Method I was, however, found to have several inherent disadvantages. The injection needle sometimes passed through the opposite wall of the artery with consequent

extravascular deposition of the contrast medium. Animals in which this occurred were discarded. The hyperaemia following the injection was often retarded and patchy. Gross infarction was not uncommon. Method I was therefore not used for later experiments.

Method II. Two ligatures were passed under the abdominal aorta, one at a level between the renal arteries and the other 4—5 cm distal thereto, below the origin of the left renal artery (Fig. 1). The proximal ligature was then lifted and blood supply to the left kidney shut off without impeding the flow to the right kidney. The contrast medium was injected into the aorta between the ligatures and thus flowed into the left kidney only.

In order to check that no contrast medium had flowed into the right (= control) kidney, roentgenograms were sometimes taken during or immediately after its injection (Figs. 1 and 2).

The ligature round the aorta was left in situ for further control at post-mortem examination. In 7 experiments (five using Umbradil 50 %, one 35 % and one 17.5 %) the ligature was inadvertently placed proximal to the origin of the right renal artery. In these cases there was thus no control kidney. The injection time was 5—15 seconds, during which 0.3—1.5 ml (average, 0.5 ml) of contrast medium was injected and the blood shut off for a further 5 seconds. Bleeding from the aorta on removal of the needle was readily controlled by gentle application of a tampon.

Method II was used on 69 animals, of which 3 were discarded because of nephritis and 1 because of aortic thrombosis. This left 65 experiments for analysis. (See Table I.)

The general condition of the animals during the experiments was on the whole good. In 2 of the experiments an increasing retroperitoneal haematoma made it necessary to interrupt the experiment after 10 and 15 minutes respectively. Bleeding from the site of the puncture was otherwise never more than negligible. In 1 case, in which Umbradil 25 per cent was used, aortic thrombosis developed at the origin of the artery and caused renal infarction.

Method III. (This material represents part of a large series being used by one of us (I.) in a roentgenographic study of renal circulation in the presence of experimental hydronephrosis.) The left ureter was ligated with consequent hydronephrosis. The parenchyma of the left kidney gradually underwent degeneration with the development of compensatory hypertrophy of the right kidney. The animals were allowed to survive for a period varying from a few days to several months. Repeated angiography, in which the contrast medium was deposited in a retrograde direction into the carotid artery, showed that the lumen of the left renal artery gradually diminished, while that of the right gradually increased. Thus, the major part of the contrast medium passed into the right kidney, which was charged with contrast medium, while the left kidney was hardly visible in the roentgenogram (Figs. 3 and 4). Angiograms were taken of each animal on about 6 occasions, 3 or 4 of which fell within the last 5—6 days before the animals were killed. The contrast medium (Umbradil 50 %) was given in a dose of 3 ml per kg bodyweight.

Method III was used on 29 rabbits (see Table IV). This method is more representative of clinical renal angiography, because the circulation is not shut off and the contrast medium is diluted in the aorta before it reaches the kidney. In addition, renal ischaemia is avoided.

All of the animals were killed by intravenous injection of air and examined immediately after death. The kidneys were inspected in situ. The position of the proximal ligature was checked (Method II). The kidneys were removed and studied for any differences. They were weighed (except in the first 11 cases), and in most cases photographs were also taken of the kidneys.

Fig. 1. Contrast medium, Umbradil 50 %, injected by Method II. The aorta and the left renal artery are visualized. No contrast medium seen in the right renal artery or right kidney.

Fig. 2. Two seconds after the blood flow is re-established, a good nephrographic effect is seen in the left kidney. The contrast medium has begun to pass into the renal vein (Umbradil 25 %).

Specimens of bladder urine from 11 of the animals in group II were examined for the presence of albumin (Heller's test). Following injection of Umbradil in concentration of 17.5 or more Heller's test was positive in 3 cases and negative in 5. The 3 animals that had albuminuria had enlarged pale kidneys showing histologic signs of damage by the contrast medium. In the remaining three animals, for which Umbradil 10 % was used, Heller's test was negative.

Control of the Methods. In the beginning of the investigation control experiments were performed on altogether 16 rabbits.

Fig. 3. Aortogram produced with Umbradil 50 % injected by Method III into an animal with left-sided hydronephrosis (the ureter had been ligated for 83 days). The left renal artery indicated by the arrow is much narrower than the right.

Fig. 4. Capillary phase, 2 seconds after the roentgenogram shown in Fig. 3. Good nephrographic effect of the right kidney, almost none of the left. Outline of the left kidney indicated by arrows.

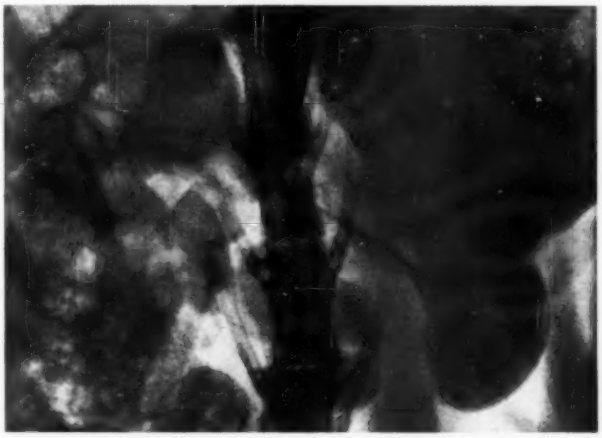


Fig. 5. The renal artery and its branches are distinctly seen in the angiogram (Umbradil 10 %).

1. *Anaesthetisation.* Anaesthesia, deeper and more prolonged than that used in the study, was induced in 4 rabbits. The animals were killed 90 minutes to 15 hours after induction.

2. *Operation.* 6 animals were operated on by Method II with the aorta shut off for 15—30 seconds at a level between the renal arteries. But the aorta was not punctured. The animals were killed 15 minutes—24 hours afterwards.

3. *Injection.* 6 animals were operated on by Method II, but normal saline was injected instead of contrast medium. The injection time was 5—25 seconds, and the aorta was shut off for 10—30 seconds. The animals were killed after 15 minutes—25 hours.

In none of the 16 animals did microscopic examination show any pathologic condition (see page 128).

It was observed that even a fairly dilute contrast medium is capable of producing morbid changes: it was therefore interesting to note that the contrast medium in 10 per cent concentration is sufficient for good roentgenographic visualisation of the renal vessels (Fig. 5). In some animals studied in connection with the authors' investigation and in which Umbradil 50 % in a dose of 3 ml/kg bodyweight was injected into the carotid artery, the concentration of the contrast medium was measured in blood specimens collected from the femoral artery. The highest concentration recorded was 19 per cent. In renal angiography ad modum SELDINGER (1953) Umbradil 60 % (20 to 50 ml, 2—3 seconds) was injected and samples were drawn from the contralateral femoral artery: a maximum concentration of 16—17 per cent was noted (IDBOHRN and JACOBSSON). (The concentration of Umbradil is calculated from the optical density of diluted serum at 2,850 Å.) FARIÑAS (1946) states that

in retrograde abdominal aortography using a 70 per cent contrast medium (20 ml 2½—3 seconds) the concentration in the aorta is about 8—10 per cent.

Results

A. Gross observations

The injection of the contrast medium immediately produced transient pallor of the kidney, which was soon followed by marked hyperaemia. When Method I was used, the ischaemia sometimes persisted for about 15 minutes. At post-mortem examination the kidney showed both hyperaemic and anaemic patches, probably attributable to the injection of air intravenously. The kidneys were often swollen and pale, and when the animals were killed within 24 hours of the last injection, the cut surface was often bulging. Infarcts were seen in 1 animal with an aortic thrombus and in 3 in which the contrast medium (50 per cent) had been injected directly into the renal artery. Sometimes the cortex was pale and stood out distinctly against the hyperaemic medulla.

The degree of renal enlargement, as judged by increase in weight, was compared with the concentration of the contrast medium used. On injection of a contrast medium in a concentration of more than 10 per cent, the left kidney was usually 1—2.5 gm. heavier than the right at postmortem examination. Furthermore the most pronounced histologic changes were seen in those left kidneys that were enlarged most.

In many of the experiments the kidneys were studied roentgenographically post mortem, but no contrast medium could be demonstrated in kidneys of those animals that were killed more than 2 hours after the injection of the medium. Therefore, no evidence was available to suggest that the contrast medium injected is retained in the kidney.

B. Histologic studies

Technique. After the kidney had been weighed it was fixed as quickly as possible — one half of the kidney in Carnoy's solution and the other half in 10 per cent formalin. The halves were first cut into 1—3 mm slices in order to secure quicker and more even fixation. The preparations — at least 2 thick slices from each half of the kidney — were embedded in paraffin and cut into 6 μ sections. These were stained according to v. Gieson, with haematoxylineosin and with periodic-acid Schiff reaction according to McMANUS (1950).

Controls. The right kidney of all animals was studied. Of these, only those exposed to the contrast medium showed any signs of damage. The kidneys of the 16 controls did not show any signs which made it difficult to assess the type or extent of the damage due to the contrast medium. Exudative changes were not seen in Bowman's capsule. Scattered convoluted tubules showed finely granular casts of irregular shape. They were stained yellow-green with v. Gieson and were slightly basophilic. They were never asso-

ciated with any widening of the lumen or epithelial injury. Eosinophilic cylinders with a few intermingled cells were seen far out in the papillary ducts. These appearances may thus be regarded as normal.

The Histologic Appearance of Injury due to the Contrast Medium. The following description refers to kidneys of rabbits used for Methods I and II, then only to those in which concentrations of 17.5 per cent or more of the medium were used, *i. e.* the concentrations that caused injury. The earliest change observed was that some of the glomeruli were strikingly hyperaemic with dilated capillaries. Fairly distinct changes appeared within 5—18 minutes. Bowman's capsule became filled with albuminous exudate, which produced a marked widening, but did not cause compression of the glomeruli. The exudate stained like blood plasma, showed the same type of vacuolation and was initially free from granulation or cellular elements. Some hours later isolated leucocytes were seen in the glomerular capillaries, but never in the exudate. This type of change never persisted more than 3 days, but was commonest in those kidneys examined within 10 hours. Within 15 minutes, at times large parts of the tubules while at other times only the most proximal parts of the nephron were filled with albuminous exudate.

The morphologic changes soon reached their maximum. The appearances noted after 1—24 hours was dominated by this type of exudation. Large regions of the nephrons showed widened tubules more or less filled with exudate. Fig. 7 illustrates these changes in various segments. In the proximal convoluted tubules the vacuolated exudate was of the same appearance as that described above (Figs. 6 and 7a). In the distal con-

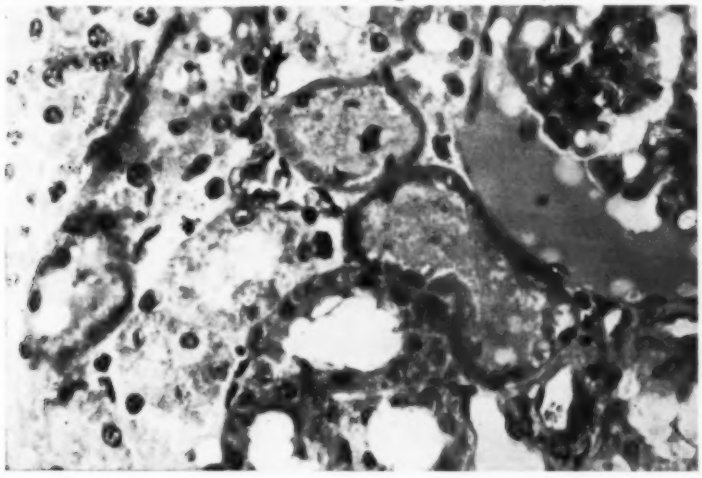
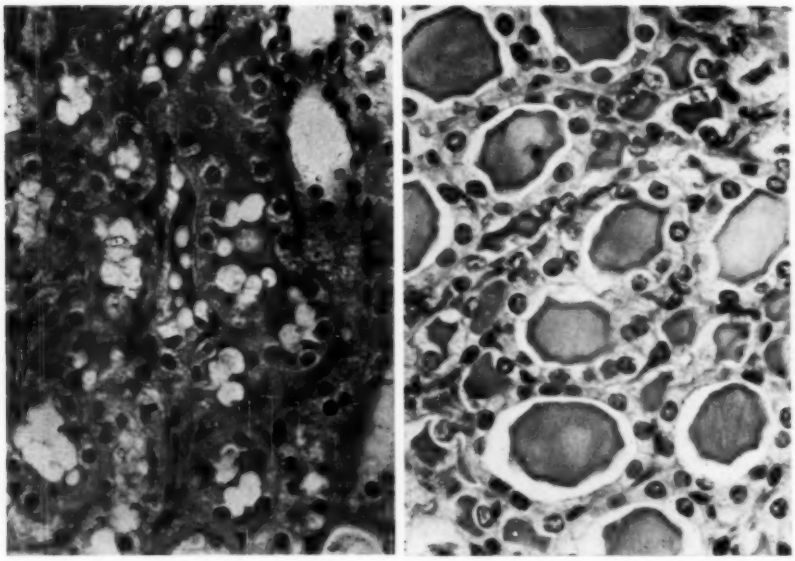


Fig. 6. One hour after injection of Umbradil 50 %. Exudate in the capsular space and adjacent tubules. Commencing degeneration of the epithelial cells. Glomerulus in right upper corner.



a. b.

Fig. 7. Two hours after injection of Umbradil 50 %. a. Characteristic, vacuolated exudate and traces of hyaline drop degeneration in the proximal tubules. b. Fairly compact cylindrical casts are seen in the tubules.

voluted tubules, in Henle's loops and in the collecting tubules the exudate tended to assume the appearance of hyaline casts, *i. e.* on fixation it left a narrow free margin along the epithelial cells. Moreover, no vacuoles were seen and the exudate showed eosinophilia and was clearly stained according to McManus. In the dilated tubules the epithelial cells became flatter and flatter, and cells were desquamated and carried off by the exudate. The desquamation was pronounced even after a few hours. The extent of these changes varied from one kidney to another, sometimes the major part of the kidney was involved, sometimes only a single nephron.

As early as 1 hour fairly distinct degenerative changes were seen. In small segments of the tubules the epithelial cells of the kidney showed pyknotic nuclei, fragments of the cells were shed into the lumen, and more granular casts formed and completely filled the tubules. This type of degeneration is illustrated in Fig. 8. During the following 2—48 hours these changes progressed. They will be referred to as epithelial necrosis. In the early stages the necrotic foci were surrounded by a sparse accu-

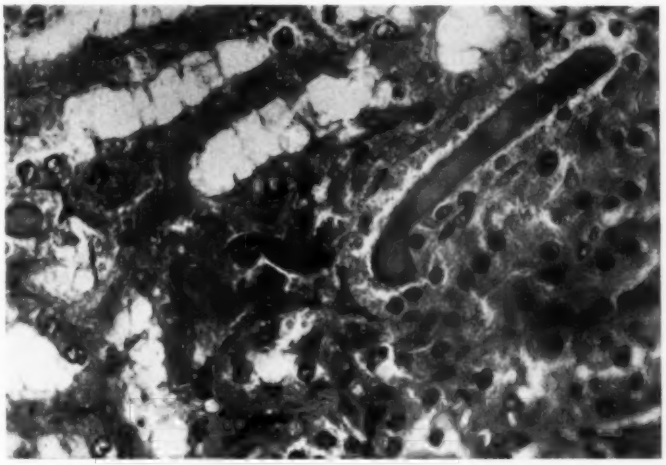


Fig. 8. Twelve hours after the injection of Umbradil 35 %. Necrotic foci in the cortical tubules with destruction of the epithelial cells.

mulation of leucocytes, which, however, soon disappeared and never dominated the picture (except in the presence of true infarction — see below).

Epithelial necrosis was seen both in the cortex and medulla. It was usually most advanced in the distal convoluted tubules and in the thick part of Henle's loops.

Hyaline drop degeneration, most pronounced 10—20 minutes after the injection, was seen in the epithelial cells of the proximal convoluted tubules. These cells were filled with spherical droplets of varying size. The droplets stained in the same way as the intraductal exudate, but in this segment the exudate was scanty. This type of change was usually seen in kidneys in which the damage was severe enough to cause epithelial necrosis, but the outlines of these particular cells were distinct. The changes are illustrated in Fig. 9. The appearances of this drop degeneration is exactly the same as that produced on the injection of albuminous substances of low molecular weight, but is also seen in the presence of certain types of toxic injury (ALLEN and others). The renal epithelium showed no signs of fatty degeneration.

Regression of Changes and Sequelae. Most of the changes described subsided considerably within 24 hours, but epithelial necrosis persisted longer. In animals with this type of injury marked regeneration was observed after 2—4 days. Epithelial cells with basophilic cytoplasm

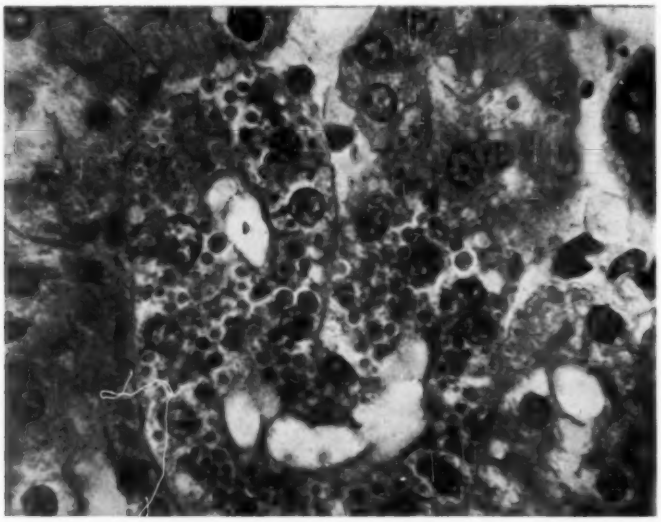


Fig. 9. Ten hours after injection of Umbradil 50 %. Marked hyaline droplet degeneration of the proximal tubules.

lined the walls of the tubules. The cells were low, undifferentiated, but stained distinctly and sometimes abundant mitoses were seen. Mitoses were seen both in the cortex and in the medulla (Fig. 10). The exudative changes gradually decreased and the epithelial cells became higher and more differentiated. These extensive changes disappeared within 5—10 days. However, a few segments of the tubules showed fairly basophilic epithelial cells, and here and there cylinders persisted. The morphologic appearances of the kidneys were otherwise normal. In only 1 kidney small segments of the ducts showed small foci of calcified epithelial necrosis. (Fig. 11.)

It is thus clear that most of the renal injuries were reversible and, morphologically, they usually healed completely. Kidneys examined 3 days or more after the injection often showed only insignificant changes. It was not always possible to judge the effect of the contrast medium in those animals that were allowed to survive so long, because any lesions produced might have healed in the meantime. Nevertheless, the changes observed strongly suggest that regeneration is rapid. An exception to this rule was in the case of infarction. The histologic appearances even within an hour showed confluent regions of epithelial necrosis, often

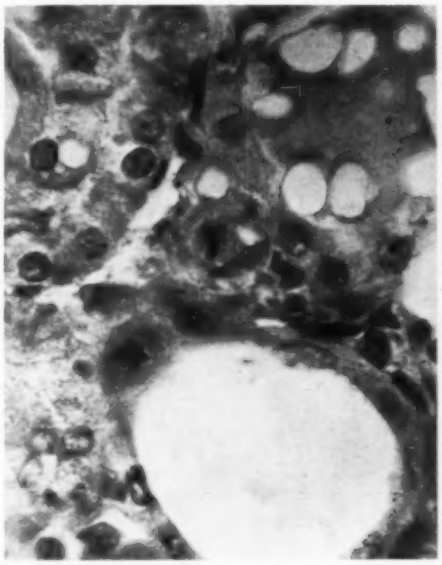


Fig. 10. Signs of regeneration. Mitoses in the cortex 3 days after injection of Umbradil 50 %. Unusually abundant exudate persists in the tubules.

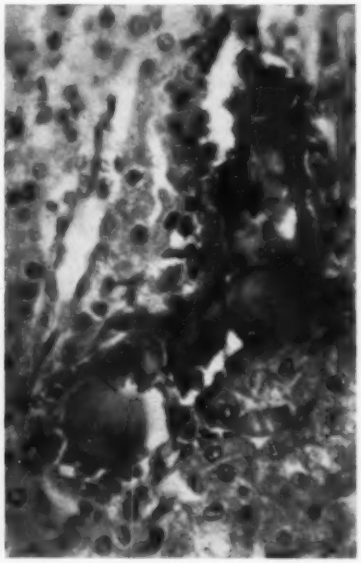


Fig. 11. Calcification in one case indicating calcified epithelial necrosis of the cortex five days after injection of Umbradil 50 %.

surrounded by a fringe of leucocytes. Morphologically the picture conveyed the impression of confluent necrotic foci, localised mainly to the cortex. Despite careful search no thrombi were seen in the vessels. It was thus not possible to say with certainty what had caused these necrotic lesions.

C. Relationship between the Severity of Renal Injury and Concentration of the Contrast Medium

In order to get an idea of the types and course of injury following various concentrations of the contrast medium, the animals were killed at a varying interval after the injection. For purposes of comparison the series were divided into three groups according to the interval between the injection of contrast medium and examination of the kidneys (Table II). Although attention was directed mainly to the presence or absence of renal injury, the occurrence of epithelial necrosis and infarcts was also noted. Animals killed within 18 minutes of the injection were not acceptable for this comparison, first because it is difficult to judge the severity of any injury with certainty and, secondly, a practically

normal picture so early after the injection does not exclude the possibility of later changes. This assumption is strengthened particularly by the observations made in the animals used for Method I (top row in Table II).

Table II

Frequency of different pathologic changes following injection of contrast medium in various concentrations

Conc. Umbradil	5—18 minutes		1 hour—3 days				More than 3 days	
	Injury	No injury	Infarct	Epithelial necrosis	Nephrosis only	No injury	Injury	No injury
50 %[1]	4[2]	5[2]	7	6	2	0	2	0
50 %	4	4	0	10	4	2	4	1
35 %	4	0	0(1)[3]	4	0	2	—	1
25 %	2	0	0	5	2	0	—	—
17.5 %	3	1	0	5	2	2	0	2
10 %	—	—	0	0	0	8	—	—

[1] According to Method I, others according to Method II. — [2] No. of kidneys. Sometimes both kidneys of one and the same rabbit were studied at different periods after the injection. — [3] Aortic thrombosis.

The lesions that appeared from 1 hour to 3 days after the injection were grouped according to severity, because both epithelial necrosis and desquamation were obvious within this interval. In those animals that were not killed until the third day after the injection, the injuries, if any, would have healed completely. These exclusions render the number of animals examined within each concentration group rather small, but, on the other hand, the groups are more homogeneous.

A striking observation made on analysis of the lesions recorded in the animals used for Method II in Table II was that the frequency of the various types of injury did not appreciably vary with the concentration of the contrast medium used when above 10 per cent (compare 50 + 35 with 25 + 17.5 per cent). Each of these concentrations was thus capable of causing epithelial necrosis. Neither did the frequency of intact kidneys vary with the concentrations. The extent of the epithelial injury in the kidneys is given in Table III. One might have expected that at least the extent of the injury might vary with the concentration of the contrast medium, but no such definite relationship could be demonstrated (compare groups 17.5 + 25 per cent with 50 per cent). It is also clear from the table that these necrotic foci varied in situation from one animal to another, but were usually most pronounced in the medulla. Another observation of interest was that the increase in weight of the kidney varied with the extent of the region involved by the necrotic foci. However,

Table III

Severity of renal injury (severity of epithelial necrosis) Method II 1 hour to 3 days after injection

Contrast medium Umbradil	Rabbit No.	Cortex	Medulla	Interval between injection and examination	Contrast medium Umbradil	Rabbit No.	Cortex	Medulla	Interval between injection and examination
50 %	42[1]	1	1	14 hours		46	2	5	12 hours
	66	1	1	21.5 »		45	(4	6[2])	14 »
	65	2	1	23 »	25 %	67	2	—	1.5 »
	41	1	3	10.5 »		79	3	4	1 day 22.5 hours
	36	1	4	15 »		84	2	5	20 hours
	32	3	2	16.5 »		78	3	5	13 »
	28	4	2	13 »		93	3	5	12.5 »
	64	2	4	2 »	17.5 %	77	—	1	14 »
	59	1	5	22.5 »		98	—	1	2 »
	37	3	5	13 »		76[1]	1	2	23 »
35 %	47	1	1	11 »		82	1	3	1 day 17.5 hours
	35	1	1	2.5 days		91	3	4	22.5 hours

The damage was graded according to the appearance of the epithelial necrotic foci. Grade 1 was said to denote isolated epithelial necrotic foci, 2 few, 3 moderate, 4 several, 5 widespread, 6 confluent (= infarct).

[1] Contrast medium was injected into both kidneys. — [2] Thrombus in aorta.

no correlation was found between the increase in weight and the concentration of the contrast medium.

These results thus suggest that exposure of the kidney to a contrast medium in a concentration exceeding a critical level lying between 10 and 17.5 per cent is capable of causing tissue injury and that the severity, type or frequency of such injury does not appreciably vary with varying concentration above this critical level.

D. Renal Injury following Repeated Injection of Umbradil 50 %

In the experiments using rabbits with leftsided artificial hydronephrosis the renal angiograms showed a considerable accumulation of contrast medium in the right kidney. At post-mortem examination they were found to be enlarged and often markedly hyperaemic. Sometimes small, old or recent infarcts were seen in the kidney. The observations made in 3 series of animals with artificial hydronephrosis are summarised in Table IV. Microscopic examination showed varying, often extensive injury of the types described above. In the 1948 series the kidneys were not cut before fixation (10 per cent formalin) and sometimes the presence of slight tissue changes could not be excluded. The frequency of

Table IV

Renal injury following injection of Umbradil 50 % in the hydronephrosis group (right kidney)

Injury		Series 1948	Series 1949	Series 1950—51
Epithelial necrosis		0	1	2
Nephrosis		1	2	5
Normal	Uncertain	9[1]	1	2
	Certain	—	5	1
Total sum		10	9	10

[1] Fixation less satisfactory.

injury was, however, much lower in this series than in the 1950—51 series. In the latter the amount of contrast medium used was as a rule smaller but was injected at a quicker rate and more angiograms were taken, especially during the last few days before the animal was killed. The table suggests that the risk of fairly extensive injury grows with an increasing number of injections and increasing injection pressure. These injuries thus occurred despite the fact that the contrast medium was diluted to a certain extent with the aortic blood.

Discussion

There is much to suggest that the lesions demonstrated in these animal experiments were of multiple origin. The kidneys were exposed to ischaemia, to a toxic action of the anaesthetic and to a contrast medium in varying concentration. Although some of these factors are not capable, by themselves, of causing demonstrable injury, they may render the tissue more vulnerable to the action of the contrast medium. Thus cholaemia will produce a more pronounced nephrosis if the kidney has suffered even brief ischaemia (Fajers 1953). In clinical renal angiography multiple factors must also be considered. The examination is often performed under anaesthesia and the kidneys are often the site of more or less serious injury such as infection, hydronephrosis, tumour or cyst. According to Smith (1951), the undesired effect of ether anaesthesia on the kidneys is greater in rabbits than in man.

A striking observation made in the present investigation was the variation in sensibility of the animal, although repeated injections of contrast medium was followed by injury in a large percentage of the animals (Method III). No explanation can be offered for the wide individual variation, which might, however, serve as a warning: the fact that the injection of contrast medium does not usually cause any demonstrable

injury does not exclude the possibility that it might sometimes cause severe damage. When the contrast medium was directly injected into the renal artery, the injury produced was more severe and appeared more regularly. Even if we disregard renal infarction, which may be due to technical measures used in the experiments but not applied clinically, all of the animals showed frank renal injury. It sounds less likely that the variation in the effective concentration can explain the wide variation between the animals treated by Method II. No correlation was found between the extent or frequency of renal injury and the injection time and thereby the amounts of contrast medium of each concentration used. The individual variation is probably ascribable to the variation in duration of the effect of the contrast medium and of the ischaemia. Repeated renal angiography also showed that injection of contrast medium is followed by marked vascular spasm (Method III).

The morphologic examination showed renal injury with a severe, but transient disturbance of the permeability of the glomeruli with exudation of plasma proteins in the tubules. The following observations suggest that the exudate consisted of serum proteins: Stainability and vacuolisation corresponded to that of blood plasma. The appearance of the lesions in the tubules was the same as that of protein nephrosis (hyaline droplet degeneration). Heller's test showed the presence of albumin in urine from a few of those animals which had received contrast medium in a concentration of 17.5 per cent or more.

That the exudate found in the kidneys contained only a negligible quantity of contrast medium was proved by the roentgenograms of kidneys removed from animals used for Method II and killed at varying intervals after the injection.

Another interesting observation was that increasing the concentration of the contrast medium above a critical level lying somewhere between 10 and 17.5 per cent was not accompanied by an increase in the severity of the injury produced. The absence of any definite relationship between the severity of renal injury and the concentration argues against a direct toxic effect of the contrast medium on the epithelial cells, and for a more complex cause.

The renal injury can be assigned to the heterogenic group of injuries classed under the heading tubular nephrosis. Neither granulomas nor severe tubular lesions (tubuli-rhexis) were observed. According to ALLEN (1951), hyaline droplet degeneration is characteristic of proximal nephron nephrosis, but it was seldom seen in the present series. In the earlier stages the changes bore appearances similar to those described by FRENCH (1950) for 'glomerulonephrosis' and disturbed permeability in the glomerular loops seems to be an important component of the damage in our series. The quick restitution (at any rate morphologically) is understand-

able in the absence of any contrast medium or deposition of pigment or crystals in the renal epithelium or cylinders. The latter appear to consist of an albuminous exudate plus desquamated epithelial cells. The contrast medium is very hypertonic but the renal injury shows no features similar to those seen in osmotic nephrosis (HELMHOLTZ 1933, LINDBERG et al., 1939, and others).

It was interesting to compare the type of the renal injuries with that of the lesions observed by BROMAN and OLLE OLSSON (1948, 1949) in their experimental study of the tolerance of the vessels to contrast medium in cerebral angiography. They found Umbradil 50 % to cause a transient disturbance of the permeability of the blood-brain barrier. Of the contrast media studied by them (Umbradil, Umbradil forte, Dijodon (35 and 50 %) and Ioduron 30 %) all except Umbradil produced haemorrhages, marked oedema or stasis. On later investigation of the effect of contrast medium injected into the cerebral vessels damaged beforehand with a toxic agent, BROMAN, FORSSMAN and OLLE OLSSON (1950) noted that even lower concentrations of contrast media are capable of injuring such vessels. An important feature of the renal injury from the contrast medium appears to be transient disturbance of the permeability of the glomeruli and thus of the same type as that in the CNS. Of these two organs the kidney seems to be more susceptible.

Of other contrast media used clinically, Dijodon and Uroselectan B have been studied for their effect on the kidneys in experimental animals. SCRUFARI and DALLA POZZA (1949) found Dijodon to produce changes consisting of transient swelling of the tubular epithelium, glomerular ischaemia and small discrete interstitial haemorrhages, but no changes of the type observed in the present experiments employing Umbradil. BACCAGLINI and BALLARIN (1940), who used Uroselectan B, reported damage similar to that following the use of Dijodon. The epithelial changes corresponded in appearance to those of osmotic nephrosis. They have been described by ALLEN as being without evidence of renal dysfunction. Unlike the lesions caused by Umbradil in our experiments the injury produced by Uroselectan B varied with the concentration of the contrast medium. Neither Dijodon nor Uroselectan B was studied in the present investigation, and as the methods used by SCRUFARI and DALLA POZZA and by BACCAGLINI and BALLARIN differed from those used by us, closer comparison of the results is hardly possible. According to Methods I and II of the present investigation, the blood supply to the kidney was shut off: this permitted a closer estimation of the concentration of the contrast medium in the kidney, and consequently facilitated the evaluation of the injurious effect of the various concentrations. SCRUFARI and DALLA POZZA ligated the aorta of a few of their animals, and then evidently proximal to the right renal artery, so that neither

kidney could be used as a control. As a rule they did not ligate the aorta, and therefore the concentration of the contrast medium in the actual kidney could not be assessed with certainty.

The conditions used in these experiments are not strictly comparable to clinical conditions. The contrast medium is diluted in the blood stream, and the concentration in the renal artery will vary within a wide range. In a few instances the concentration of the contrast medium in the femoral artery was determined after injection of Umbradil 60 % (30—40 ml, 2—3 seconds) in renal angiography. The maximal concentration recorded was 16—17 per cent. If the tolerance of the rabbit's kidney can be taken as representative of that in man, this value is in the region of the minimum toxic concentration recorded.

The damage observed in the rabbit's kidneys following injection of Umbradil in the present investigation and the observations made by earlier workers in this field and referred to above suggest that caution should be exercised in the employment of renal angiography. Two factors should especially be borne in mind:

1. Methods permitting the deposition of a contrast medium of a concentration intended for the aorta directly into the renal artery must be risky, because the concentration of the contrast medium in the kidney then exceeds non-toxic concentration.

2. Observations made in experiments using Method III suggest that renal angiography, if repeated at short intervals, may cause damage to the kidney with a quantity of contrast medium, too small by itself to cause renal injury.

The radiologic part of the investigation was carried out by IDBOHRN and the histologic studies by BERG.

SUMMARY

Umbradil forte (50 %) and Umbradil, both undiluted and diluted, were used in an investigation of the tolerance of the rabbit's kidney to the contrast medium in renal angiography. In many of the animals a concentration of 17.5 per cent or more in the renal artery produced toxic injury of the kidney with exudation and degeneration, especially of the tubules. Above this critical level the extent and severity of the damage were not found to be correlated with the concentration of the contrast medium. The changes were, as a rule, reversible.

ZUSAMMENFASSUNG

Umbradil forte (50%ig) und Umbradil wurden unverdünnt und verdünnt bei einer Untersuchung der Toleranz der Kaninchenniere gegenüber diesem Kontrastmittel be der renalen Angiographie benutzt. Bei vielen Tieren verursachte eine Konzentration in der Nierenarterie von 17.5 % oder mehr Nierenschädigungen mit Exsudation und Degeneration, besonders der Tubuli. Oberhalb dieser kritischen Grenze konnte eine Korrelation zwischen der Konzentration des Kontrastmediums und der Ausbreitung und Schwere

der Schädigung nicht beobachtet werden. Die Veränderungen waren in der Regel reversibler Natur.

RÉSUMÉ

L'Umbradil forte (50 pour cent) et l'Umbradil, purs et dilués, ont été utilisés pour des recherches sur la tolérance du rein du lapin au produit de contraste pour angiographie rénale. Chez la plupart des animaux, une concentration de 17.5 pour cent ou plus dans l'artère rénale a produit une atteinte toxique du rein avec exsudation et dégénérescence, en particulier des tubes. Au-dessus de cette concentration critique l'étendue et la sévérité des lésions n'ont pas semblé en rapport avec la concentration du produit de contraste. Les lésions ont été, en règle générale, réversibles.

REFERENCES

ALLEN, A. C.: The kidney — medical and surgical diseases. Grune & Stratton Inc., New York 1951.

BACCAGLINI, G. and BALLARIN, G.: L'aortografia con mezzi di contrasto. Radiol. Med. 27 (1940), 1.

BROMAN, T. and OLSSON, OLLE: The tolerance of cerebral blood vessels to a contrast medium of the diodrast group. Acta radiol. 30 (1948), 326.

— Experimental study of contrast media for cerebral angiography with reference to possible injurious effects on the cerebral vessels. Acta radiol. 31 (1949), 321.

BROMAN, T., FORSSMAN, B. and OLSSON, OLLE: Further experimental investigations of injuries from contrast media in cerebral angiography. Acta radiol. 34 (1950), 135.

DUCUING, J., PONS, H. and ENJALBERT, A.: L'aortographie abdominale (technique, incidents et accidents, indications, iconographie). J. Radiol. et d'électrol. 30 (1949), 497.

FAJERS, C.-M.: Personal communication 1953.

FARIÑAS, P.: Retrograde abdominal aortography. Radiology 47 (1946), 344.

FRENCH, A. J.: Glomerulonephrosis: morphologic manifestation of cortical ischemia in toxic oliguria and lower nephron nephrosis. Arch. Pathol. 49 (1950), 43.

HELMHOLTZ, H. F.: Renal changes in the rabbit resulting from intravenous injections of hypertonic solution of sucrose. J. Pediat. 3 (1933), 144.

HENLINE, R. B. and MOORE, S. W.: Renal arteriography. Am. J. Surg. 32 (1936), 222.

IDBOHRN, H. and JACOBSSON, K.: To be published in Acta Radiol.

LARSSON, H. and PALMLÖV, A.: Abdominal aortography with special reference to its complications. Acta radiol. 38 (1952), 111.

LINDBERG, H. A., WALD, M. H. and BARKER, M. H.: Renal changes following administration of hypertonic solutions. Arch. Int. Med. 63 (1939), 907.

MCMANUS, J. F. A.: Medical diseases of the kidney. Lea and Febiger, Philadelphia 1950.

OSELLADORE, G.: Di una nuova tecnica per esequire l'aortagrafia. Atti Soc. med.-chir. Padova 15 (1937), 143.

SCRUFARI, V. and DALLA POZZA, M.: Contribute sperimentale alla studie della nefrangiografia. Urologia, Treviso (1949), 525.

SELDINGER, S. I.: Catheter replacement of the needle in percutaneous arteriography. Acta radiol. 39 (1953), 368.

SMITH, H. W.: The kidney. Structure and function in health and disease, p. 446. Oxford Univ. Press 1951.

SMITH, P. G., RUSH, T. W. and EVANS, A. T.: The interpretation of translumbar arteriograms. J. Urol. 66 (1951), 145.

WAGNER, F. B. and PRICE, A. H.: Fatality after abdominal arteriography: prevention by new modification of technique. Surgery 27 (1950), 621.

FROM THE ROENTGEN DEPARTMENT I (DIRECTOR: DOCENT GUNNAR JÖNSSON), SÖDERSJUKHUSET, STOCKHOLM, SWEDEN

UNUSUAL CORONARY BRANCH IN A CASE OF COARCTATION

by

L. Di Guglielmo and *M. Guttadauro*

The introduction of radio-opaque substances into the study of the cavities of the heart, the great blood vessels and the pulmonary and systemic circulations, has revealed the existence of several anomalies hitherto little known, even anatomically.

In the following we describe the finding of an unusual coronary vessel visualized in the course of a thoracic aortography.

Case Report

G. K. E., male, aged 30. The family history was irrelevant. At the age of 15, attacks of slight breathlessness and giddiness which disappeared after a short time. At 25, paraesthesias in the legs apparently associated with physical exertion.

At the age of 26 he was admitted to a hospital and found to be suffering from aortic coarctation. This was followed by a period in which he felt quite well.

In October 1952, because of occasional headache and slight sensation of weakness in both legs, the patient was admitted to this hospital for further investigation.

On physical examination pulsations were visible and palpable in the supra- and infraclavicular fossae, in the axillary regions and in the fossae supraspinosae. Blood vessels could also be felt in the interscapulary regions. Systolic murmur of medium intensity, loudest over the 2nd right intercostal space. Second aortic sound accentuated.

Blood pressure: both arms, 155/70—60; both legs 105/85—75. *Oscillography* in arms and legs: typical of coarctation of the aorta. *Electrocardiogram:* Left branch block with diphasic terminal phase, as often seen in aortic coarctation. *Ocular fundus:* the arteries appeared tortuous as in severe aortic coarctation.

Radiologic examination of the heart: the total cardiac volume was 750 cc and 430 cc per square meter of body surface. Enlargement of the left ventricle. No pulmonary congestion. The upper mediastinum was deformed as in aortic coarctation. There were rib notchings on both sides.

Submitted for publication, January 15, 1954.

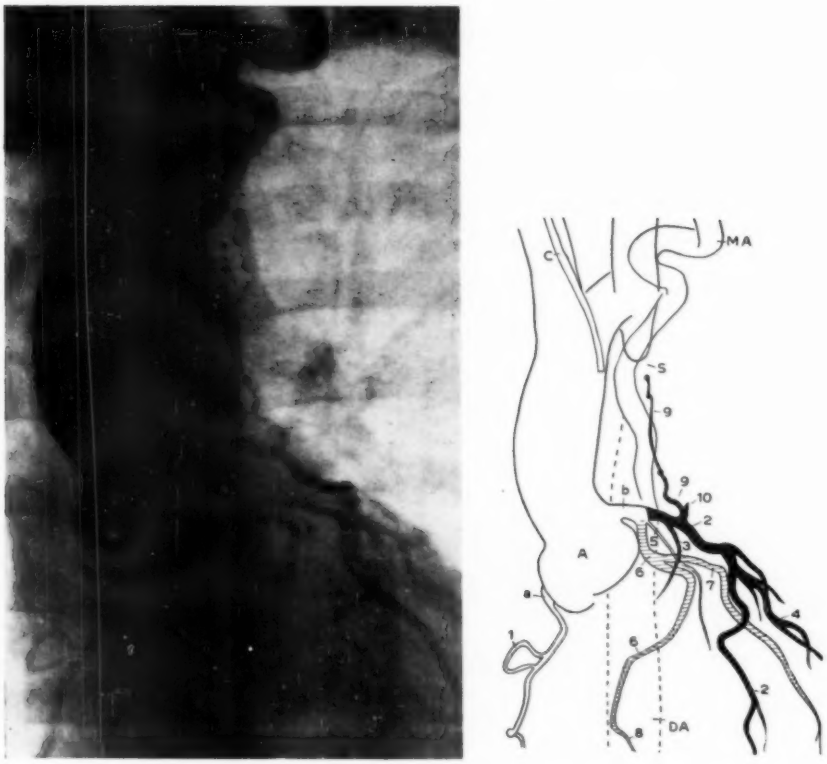


Fig. 1. *Thoracic aortography.* A-p projection. A = aortic bulb; C = catheter; S = stenosis; DA = descending aorta; MA = left internal mammary artery.
a = *right coronary artery;* 1 = anterior branch to the right ventricle; b = *left coronary artery;* 2 = anterior interventricular branch with (4) the first left branch; 3 = left conus branch; 5 = median or diagonal branch; 6 = circumflex branch; 7 = branch to the obtuse margin; 8 = posterior interventricular branch; 9 = supernumerary ascending artery, arising from the anterior interventricular branch, with (10) a slender ramification.

Thoracic aortography: a catheter n. 10 F was introduced from the right radial artery until the tip reached the level of the middle third of the ascending aorta. 75 ml of Umbradil 70 % were injected in 2 seconds and 30 roentgenograms in the antero-posterior and lateral planes simultaneously obtained in a period of 8 seconds: 12 in the first 2 seconds and then 18 in 6 seconds.

The maximal degree of stenosis was situated about 2 cm beyond the origin of the left subclavian artery. It was about 0.5 cm long. The aorta was small below the stenosis. The ascending aorta was markedly dilated having a diameter of 4 cm as measured in the films. The middle part of the arch had a diameter of 2 cm, the diameter of the distal

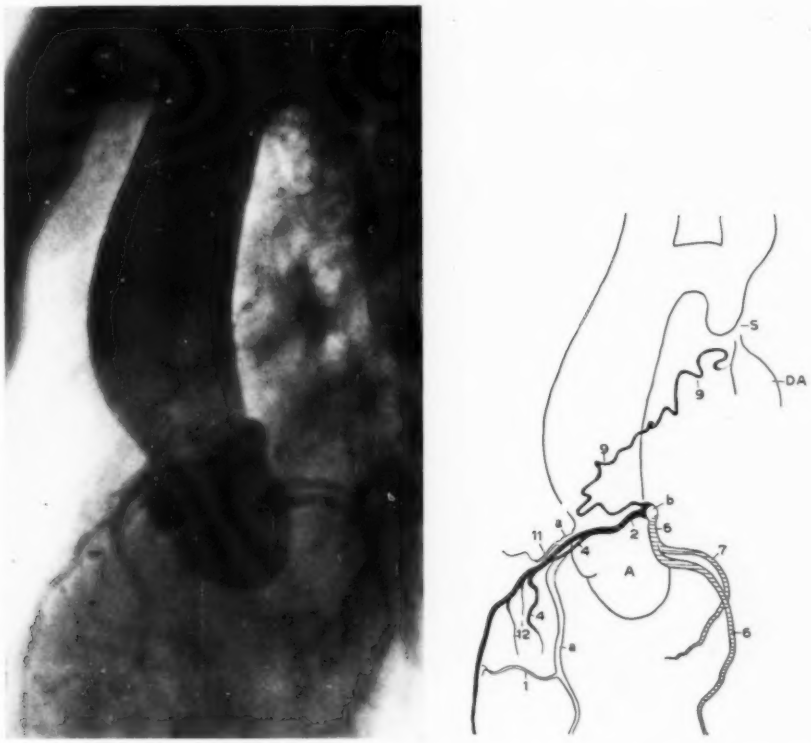


Fig. 2. *Thoracic aortography.* Lateral projection. Symbols as in preceding figure. 11 = right conus branch; 12 = anterior septal branches. Commencing slight contrast filling of some collateral vessels.

part being 1.5 cm. The left subclavian artery was very large and had a calibre of about 2 cm. The collateral system was markedly developed in the upper mediastinum.

The maximum degree of stenosis was situated at the level of the posterior part of the fifth rib.

There was good filling of the whole coronary system, both the right and the left coronary arteries being visualized. Figs. 1 and 2 show their single branches in a-p and lateral views. The whole of the left coronary artery was very highly developed. It divided into three branches and gave rise to the posterior interventricular branch usually furnished by the right coronary artery (preponderance of the left coronary artery).

Immediately after the commencement of visualization of the coronary arteries, we observed the filling of a blood vessel which departed from the upper contour of the anterior interventricular branch of the left coronary artery about 3 cm from the aortic origin of the left coronary artery and about 1.5 cm from the point at which the artery divided into three branches. This vessel, which had a fairly wide lumen at its point of origin, appeared to bifurcate almost immediately into a very fine branch, not clearly

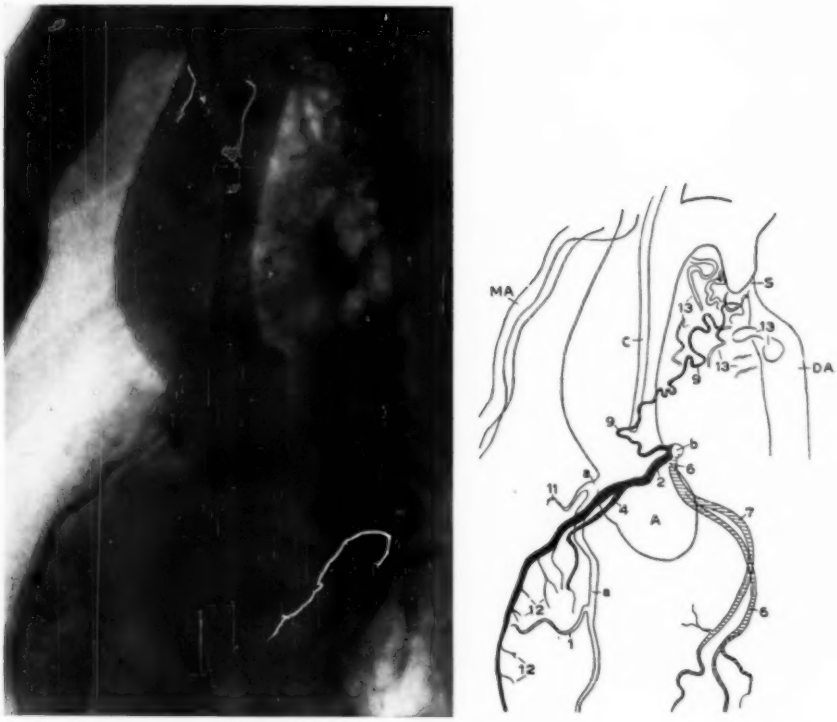


Fig. 3. *Thoracic aortography.* Lateral projection, one second later. The collateral circulation is now entirely contrast filled.

Symbols as in preceding figure. 13 = vessels of the collateral circulation.

visible in its further course, and a long ascending branch, very tortuous and with a lumen of about 1 mm. It was clearly visible in the antero-posterior and lateral films.

In the a-p projection (Fig. 1) the vessel appears to run upwards and medially. It remains distinctly separate from the ascending aorta throughout its entire length and is easy to identify right up to a point situated a little below the stenosed part of the aorta.

In the lateral projection (Fig. 2) the vessel starts from the upper margin of the anterior interventricular branch and runs at first forwards then pursuing a very tortuous course it turns upwards and backwards and may be followed to the region of the anterior contour of the descending aorta at a point just below the stenosis.

This vessel is clearly visible in 16 radiographs. It held the opaque medium for about 3 seconds. It was immediately visualized, that is, simultaneously with the aortic bulb and the first part of the coronary artery, while the main collateral circulation became contrast filled only after the 6th radiograph, *i. e.* about one second later. During that interval the vessel was visible without any superimposed shadow whatsoever.

It was possible to observe that the contrast medium moved from below upwards, *i. e.* from the left coronary artery towards the descending aorta.

In Fig. 3 (14th radiograph, lateral projection) the vessel is better contrast filled, but its terminal portion is not visible because of the superimposed collateral circulation.

Discussion

The case under consideration is one showing the whole clinical and radiologic symptomatology typical of aortic coarctation. The left coronary system is highly developed with a division into three branches and a moderate degree of preponderance. Moreover, a long branch coming from the anterior interventricular branch runs towards the descending aorta below the stenosis and may take part in the collateral circuit.

The fact that this branch is well visualized in 6 radiographs taken before the collateral circuit is filled, enables us to exclude the possibility that the findings were due to false images produced by superimposed other formations of the collateral circuit.

In the course of our studies on the arteriography of the coronary arteries we have seen 116 cases of aortic coarctation but have never encountered appearances similar to these.

A careful search of the literature shows that while anomalous origins and divisions of the coronary arteries have been observed in aortic coarctation (ABBOTT, EVANS), no author has ever, in this condition, reported a connection between the coronary arteries and the collateral circuit. MOTTURA (1942) in his exhaustive study of the collateral circulation in aortic coarctation writes: "The coronaries are the only branches of the aorta located above the stenosis which in no way participate in the collateral circuit."

In 1938 NEUMANN described two arteries which start from the coronary arteries — or more commonly from their auricular branch — turn upwards and feed the aortic wall. There should be one on the right and one on the left side and, through their ramifications, spread over the whole of the ascending aorta and the larger part of the arch. The author called them the *cardio-aortal arteries*.

These studies were taken up by KOECHER (1941), CONTI (1941), ZIMMERMANN (1941), BINI (1942), LAURENT (1944), MURATORI (1946), ROMUALDI (1947) and STRAMIGNONI (1950). By injecting and dissecting anatomic specimens all these authors were able to confirm the existence of the right cardio-aortal artery which was sometimes sufficiently well developed to be clearly visible macroscopically. However, it is their unanimous opinion that a left cardio-aortal artery either does not exist or is so small as to be without significance.

On the other hand, MURATORI has shown that there is an artery on the left side completely analogous to the one on the right described by NEUMANN. This artery, however, does not spread over the aorta but rather over the pulmonary artery. Hence the author called it the *cardio-pulmo-*

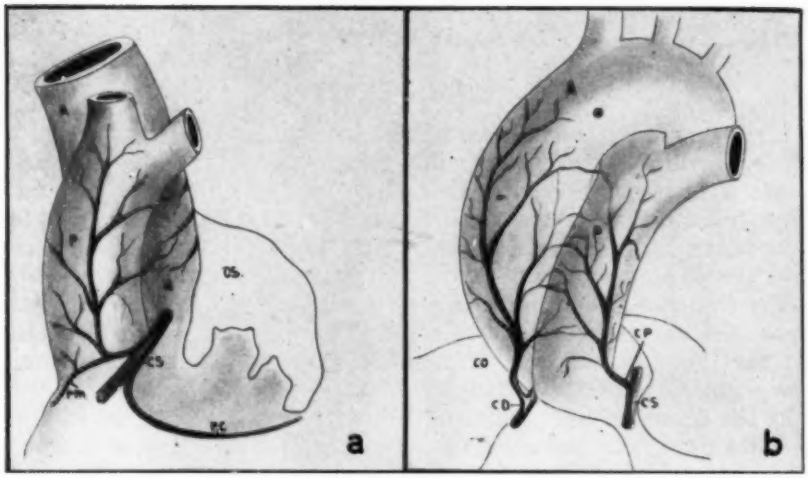


Fig. 4. The vasa vasorum of the aorta and pulmonary artery according to MURATORI. a = the cardio-pulmonary artery; b = the cardio-aortal and the cardio-pulmonary arteries. A = aorta; P = pulmonary artery; OS = left auricle; CS = left coronary artery; CD = right coronary artery; cp = cardio-pulmonary artery; ca = cardio-aortal artery; rc = circumflex branch; rm = myocardial branch. (From MURATORI).

nary artery (Figs. 4 a and b). Furthermore, the author observed that the substance injected into this artery also passed into the cardio-aortal artery, thus proving the existence of anastomoses between the two systems. This could be explained embryologically. The aorta and the pulmonary artery originate from the primitive truncus arteriosus communis. This has two nutrient arteries, one on the right and one on the left side, which anastomose. When the common trunk divides, the right nutrient artery follows the aorta (*the cardio-aortal artery*), while the left is destined for the pulmonary artery (*cardio-pulmonary artery*). Both systems, however, remain united through numerous anastomoses, even after full development.

In our case the supernumerary artery, while quite distinct from the ascending aorta, runs almost its whole course on the pulmonary artery. This is clearly visible both in the a-p and lateral projections. As there are no other anatomic formations which might explain the origin of this artery it must be the cardio-pulmonary artery described by MURATORI. In our case it is much wider than usual and this fact together with its final course suggests that it probably participates in the collateral system. Definite proof in the form of anatomic verification is, however, still lacking.

SUMMARY

A long branch of the left coronary artery running along the course of the pulmonary artery towards the descending aorta below the stenosis is described in a case of aortic coarctation. It is suggested that this branch represents the cardio-pulmonary artery described anatomically by MURATORI, and because of its course and unusually wide calibre that it may participate in the collateral circulation carrying blood from the left coronary artery to the descending aorta.

ZUSAMMENFASSUNG

Ein langer Zweig der linken Koronarterie, der längs der A. pulmonalis in Richtung Aorta descendens unterhalb der Stenose verläuft, wird in einem Fall mit einer Coarctatio aortae beschrieben. Es wird angenommen, dass dieser Zweig der von MURATORI anatomisch beschriebenen Arteria cardio-pulmonalis entspricht und dass er, auf Grund seines Verlaufes und seines ungewöhnlich weiten Kalibers, im Kollateralkreislauf mitbeteiligt sei und Blut von der linken Koronararterie zur Aorta descendens befördert.

RÉSUMÉ

Les auteurs décrivent dans un cas de coarctation de l'aorte une longue branche de l'artère coronaire gauche courant le long de l'artère pulmonaire vers l'aorte descendante, au-dessous de la sténose. Ils suggèrent que cette branche représente l'artère cardio-pulmonaire décrite anatomiquement par MURATORI, et, en raison de son trajet et de son calibre inhabituellement large, qu'elle pourrait participer à la circulation collatérale en transportant du sang de l'artère coronaire gauche à l'aorte descendante.

REFERENCES

ABBOTT, M. E.: Coarctation of the aorta of the adult type. II. A statistical study and historical retrospect of 200 recorded cases, with autopsy of stenosis or obliteration of the descending arch. Am. Heart. J. 3 (1928), 329.

BINI, G.: Contributo alla conoscenza delle alterazioni delle arterie cardioaortali (di Neumann) nel reumatismo. Arch. ital. anat. istol. pat. 15 (1942), 413.

CONTI, G.: Particolarità strutturali dei vasa vasorum della vena cava superiore e dell'aorta ascendente nell'uomo. Boll. Soc. ital. biol. sper. 23 (1941), 339.

DI GUGLIELMO, L. and GUTTADAURO, M.: A Roentgenologic Study of the Coronary Arteries in the Living. Acta radiol. Suppl. 97 (1952).

— — Anatomic Variations of the Coronary Arteries. An arteriographic study in the living. Acta radiol. 41 (1954), 393.

EDWARDS, J. E., CLAGET, T. D., DRAKE, R. L. and CHRISTENSEN, N. A.: The Collateral Circulation in Coarctation of the Aorta. Proc. Staff Meet., Mayo Clin. 23 (1948), 321.

EVANS, W.: Congenital stenosis (coarctation), atresia and interruption of the aortic arch (a study of 28 cases). Quart. J. Med. 26 (1933), 1.

KOECHER, P. H.: Die Arterielle Versorgung der Cardioaorta. Ztschr. f. microsk.-anat. Forsch. 50 (1941), 273.

LAURENT, A.: Anatomie und Pathologie der Arteria cardioaortalis. Cardiologia 8 (1944), 348.

MOTTURA, G.: Rilievi e considerazioni sulla circolazione collaterale in due casi di stenosi botalliana dell'aorta. Riv. di pat. sper. 29 (1942), 1.

MOTTURA, G.: Trasformazione elastica di arterie del circolo collaterale in casi di stenosi malformativa dell'aorta. Arch. Sc. Med. 75 (1943), 293.

MURATORI, G.: Origine, distribuzione e struttura dei vasi nutritizi dell'arteria polmonare e dell'aorta ascendente nell'uomo. Arch. Sc. Med. 82 (1946), 24.

NEUMANN, R.: Die Cardioaorta als Organ und ihr Verhalten bei Coronarsklerose. Virchow's Arch. 303 (1938), 1.

ROMUALDI: La morfologia delle arterie cardioaortiche studiata nello sviluppo e nelle alterazioni regressive in riferimento al processo arteriosclerotico dell'aorta ascendente. Arch. De Vecchi. 9 (1947), 1113.

STRAMIGNONI, A.: Sulla struttura delle arterie dette cardioaortali. Arch. Sc. Med. 90 (1950), 179.

ZIMMERMANN: Ueber den Aufbau der Cardioaorta. Zentralbl. f. allg. Path. u. path. Anat. 77 (1941), 125.

FROM RADIUMHEMMET (DIRECTOR: PROFESSOR S. HULTBERG) AND THE OTO-LARYNGOLOGIC DEPARTMENT (DIRECTOR: PROFESSOR T. SKOOG), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

CARCINOMA OF THE PARANASAL SINUSES AND THE NASAL CAVITIES

A Clinical Study of 379 Cases Treated at Radiumhemmet and the Otolaryngologic Department of Karolinska Sjukhuset, 1940—1950

by

Lars-Gunnar Larsson and *Gunnar Mårtensson*

The treatment results of malignant tumours of the paranasal and nasal cavities have been improved by the introduction of electrosurgical and radiotherapeutic methods. In Sweden the most important early work in this field was carried out by HOLMGREN and BERVEN. The exceptional value of electrocoagulation in the treatment of malignant tumours was demonstrated by BERVEN in 1920 and in 1922 HOLMGREN commenced to electrocoagulate malignant tumours of the maxillary sinus. During the next few years BERVEN and HOLMGREN developed a combined radiologic and electrosurgical method which involved preoperative roentgen therapy followed by electrocoagulation and insertion of radium tubes in the operation cavity. In 1933 ÖHNGREN reported 187 cases of malignant tumours of the maxillary and ethmoid sinuses treated principally by that method.

Since in Sweden the treatment of these tumours for the most part is centralized, a large number of patients have been referred to Radiumhemmet during the twenty years which have elapsed since ÖHNGREN's report, and in the meantime no detailed study has been undertaken with respect to the principles and results of the treatment.

The main purpose of the present investigation is to communicate the results of therapy — the combined radiologic and surgical treatment of operable cases, and the purely radiologic treatment of largely inoperable cases. The surgical treatment was carried out, with few excep-

Submitted for publication, December 31, 1953.

tions, by SKOOG and his co-workers at the Otolaryngologic Department of Karolinska Sjukhuset; the radiologic treatment at Radiumhemmet in accordance with the principles laid down by BERVEN. The clinical follow-ups were done at Radiumhemmet, where the follow-up system enabled every patient to be checked.

Definition of the Series

The investigation was limited to carcinomas arising from the mucous membranes of the paranasal sinuses and the nasal cavities. The demarcation is logical from the anatomic point of view, but may present some difficulties in practice. Especially tumours arising from the maxillary gingiva may show secondary growth into the nasal cavity or the paranasal sinuses and may be difficult to differentiate from true nasosinusal tumours. It is nevertheless our opinion that careful study of the histories and of the clinical and roentgenologic findings may enable the primary situation to be determined with a high degree of probability in the majority of cases. In a few advanced cases this demarcation was not possible but they nevertheless are included in the present series.

With regard to histologic type, the investigation was limited to carcinoma, which is the commonest malignant tumour in this region. Malignant mucous- and salivary-gland tumours were excluded with the exception of adenocarcinomas, which have a dubious relationship to mucous- and salivary-gland tumours. In some inoperable cases from the earliest years no microscopic verification was available; those patients who died within five years were included in this series. Only one case, however, lived after five years and was excluded.

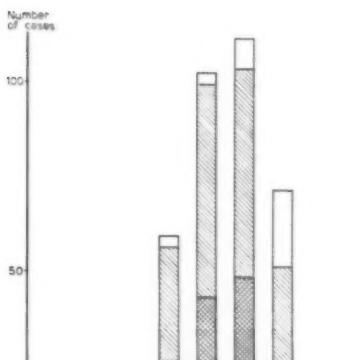


Diagram 1. Age distribution of the series. Age incidence of operated cases, cases treated by radiotherapy alone, and cases not admitted.

Composition of the Series

From 1940 to 1950 inclusive, a total of 379 patients were referred to Radiumhemmet with cancer arising from the paranasal sinuses or the nasal cavities. However, 45 of them were not admitted (Table 1). This latter group consisted of patients in whom any form of therapy was considered hopeless by virtue of advanced age, very advanced extension of the tumour, or poor general condition.

Table 1

Distribution of the Series in Time

Year	Patients Admitted	Patients not Admitted	Total
1940	30	7	37
1941	33	2	35
1942	34	6	40
1943	28	4	32
1944	32	4	36
1945	34	2	36
1946	34	6	40
1947	31	7	38
1948	21	2	23
1949	21	2	23
1950	36	3	39
	Total 334	45	379

The *age distribution* is evident from Diagram 1, which shows that these tumours were very rare up to the age of 30, and relatively uncommon before the age of 40. The youngest patient was a 19-year-old female. More than two-thirds of the series was referable to the 50 to 70 year group. The series included 188 men and 191 women, which did not indicate a predominance of the male sex as found by some authors (KIRCHNER, WATSON).

All experience shows that cancer in this region mostly arises from the mucous membrane of the maxillary or the ethmoid sinus, the former showing a marked preponderance. Due to the intimate relation between the paranasal sinuses it is often impossible to determine the primary situation. Primary carcinomas of the frontal and the sphenoid sinus are very uncommon; this series included only one case with a primary situation in the former and none in the latter sinus. In 33 cases the tumours had arisen from the ethmoid cells or the nasal cavity, and showed roentgenologically no destruction of the walls of the maxillary sinus. Fourteen of these cases were localized to the nasal cavities, with no clinical or roentgenologic lesions in the ethmoid sinus. Probably a further number of tumours had arisen from the mucous membrane of the nasal cavities, and above all the ethmoid sinus, but since the walls of the maxillary sinus were also destroyed the primary situation could not be determined.

In 155 cases the tumour was situated on the right side and in 165 on the left. Fourteen cases presented such pronounced bilateral extension that the side of the original situation was indeterminable.

Predisposing Factors

As RINGERTZ (1938) has earlier pointed out, some cases have, prior to the progressive tumour symptoms, a history of many years, with

chronic or intermittent signs of inflammatory changes in the paranasal sinuses or nasal cavities. These patients have often undergone repeated operations for commonplace sinusitis and nasal polypi. In the present series such histories were found in 48 of 330 patients whose histories could be appraised (14.5 per cent) — a figure that closely accords with that found by RINGERTZ. In 29 of these patients the symptoms of chronic sinusitis were clearly localized to one side, and the tumour had developed on the same side. Two of the patients with cancer of the nasal cavity had histories of atrophic rhinitis of many years' standing.

It seems, therefore, probable that quite a fair proportion of these carcinomas arise from mucosal changes associated with chronic inflammatory processes. This view is also supported by the relative frequency of chronic sinusitis and carcinoma in the different sinuses. Both diseases are much more frequently found in the maxillary antrum and the ethmoid than in the frontal and sphenoid sinuses. Our series also included a few examples of the more rare etiologic factors represented by certain benign growths (cylindrocellular papilloma and adenoma), which may show a conspicuous tendency to recur as well as to degenerate malignantly.

Symptoms

The local symptoms are dependent upon the situation and extension of the primary tumour. The incidence of the commonest subjective and clinical symptoms in the treated cases is summarized in Tables 2 and 3.

Table 2

Subjective Symptoms

Nature or Situation	Initial symptom percentage	Total percentage
Pain	25	51
Purulent nasal secretion	20	43
Nasal obstruction	18	38
Symptoms from the oral cavity	15	26
(dental symptoms	6.5	14)
Swelling of cheek	12	43
Sanguineous nasal secretion	8.5	30
Ocular symptoms	5	23

Table 3

Clinical signs on admission	Number of cases per cent
Asymmetry of the face	58
Tumour visible by anterior rhinoscopy	58
Tumour palpable from the oral cavity	49
One or more of the above-mentioned clinical signs	89

It is characteristic that the most frequent early symptoms (pains, nasal secretion and obstruction) were identical with the symptoms of sinusitis. The more specific tumour symptoms (tumour bulge in the face or oral cavity, dislocation of the eye, bleeding from tumour masses in the nasal cavity) are in the paranasal carcinomas signs of penetration of the bony walls and were less frequently found to be the first symptoms. Sanguineous nasal secretion is an important sign, but it occurred initially in only 8.5 per cent of the present series.

From the odontologic point of view it is worthy of note that subjective symptoms referable to the oral cavity, either in the form of a swelling in the upper jaw or dental symptoms ('toothache', loosening of the teeth), occurred in 26 per cent of the cases and represented the first symptom observed by the patient in 15 per cent. In several of these cases repeated extractions of teeth had been performed before the correct diagnosis was established.

Ocular symptoms in the form of displacement or protrusion of the eyeball, in some cases attended by diplopia, occurred in 23 per cent — in about 5 per cent as the initial symptom observed by the patient.

Roentgen examination is often regarded as the most reliable means of diagnosing malignant tumours of the paranasal sinuses. The characteristic roentgenologic tumour changes (bone destruction) are not, however, early signs in these tumours, which originate in the mucous membrane. In our series only six cases were stated to be 'without roentgenologic changes', but each of them had cancer limited to the nasal cavity. "Densities of the soft tissues alone, without signs of bone destruction" was annotated in 28 cases, and eight of these had cancer limited to the nasal cavity. The entire series accordingly included only 20 cases of sinusal cancer without roentgenologically demonstrable bone destruction, and all of these cases showed pronounced "densities" of the maxillary or ethmoid sinuses.

It must be regarded as an expression of rather late diagnosis that about 90 % of the cases on admission had clinical and roentgenologic signs of bone destruction. About 60 % of the cases had a history with progressive symptoms of more than three months and about 20 % of more than six months before the correct diagnosis was established. As the early symptoms usually were indistinguishable from the symptoms of common inflammatory conditions there are reasons to be rather pessimistic about the possibilities of improving the early diagnosis of these tumours. It is, of course, important that all physicians and dental surgeons who are responsible for the primary diagnosis should be completely familiar with the symptomatology of these tumours. It is important to realize that the early symtoms are unspecific and that a roentgen film "without signs of bone destruction" never excludes a malignant tumour.

Chronic sinusitis should not be treated conservatively for a long period, and when tissue material is removed by minor operations (removal of polyps, Caldwell-Luc operations) the material should be sent for histologic examination. In fact some of the earliest diagnoses in this series were derived from incidental findings at such operations; this seems to be the only possibility for the early diagnosis of a paranasal carcinoma.

Treatment

From the therapeutic point of view the first thing is to determine whether the tumour, in each individual case, is operable or not. From this standpoint it is important to have the services of an otologist possessing lengthy experience in this special field of tumour surgery. On primary classification in the present series the following factors were considered to contraindicate operation:

1. Advanced age. The oldest surgically treated patient in this series was aged 76, and few patients of over 70 were submitted to operation (Diagram 1).
2. Poor general condition or complicating diseases having a doubtful prognosis.
3. Roentgenologically demonstrable destruction of the base of the skull or of the pterygoid process.
4. Very extensive bone destruction or considerable bilateral spread, making radical operation highly improbable even if the base of the skull is not involved.
5. Extensive involvement of the soft tissues of the cheek or the external nose, where radical operation would entail large and disfiguring defects.
6. Tumorous infiltration of the mucous membrane in the nasopharynx.
7. Inoperable lymph-node metastases.
8. Generalized metastases.
9. Unconditional refusal by the patient. Severe mental disturbances that would make a defective condition difficult to overcome.

For natural reasons the demarcation line between operable and inoperable cases will inevitably be somewhat variable at times; of the factors enumerated above, only points 3, 6, 7 and 8 can be regarded as absolute contraindications. In the individual case there is frequently a whole problem complex, in which the final evaluation will be determined by the personal view and experience of the operator and the radiotherapeutist.

The difficulties of evaluation lay, in principle, on two different planes. First, it was a question of cases in which considerable spread posteriorly

and upwards increased the operative risks and lessened possibilities of a radical operation; and, secondly, it concerned cases which technically were quite operable without any major operative risks but in which, considering the degree of involvement, the operation was bound to cause disfiguring defects. In all of these borderline cases the principle followed in this series was to delay the final decision until full roentgen therapy had been given. This sometimes caused such regression of the tumour that the extent of surgery could be reduced, and in some cases a definitive cure was obtained by radiotherapy alone.

Technique of Radiotherapy. The radiotherapy in this series consisted partly of roentgen treatment and partly of insertion of radium according to the technique earlier described by BERVEN.

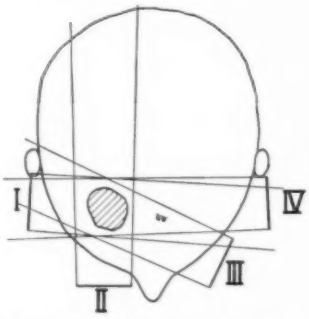


Diagram 2 a. Diagram of a cross-section of the head illustrating the typical roentgen treatment.

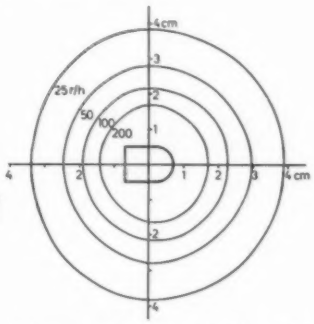


Diagram 2 b. Distribution of the dose around one of the 50 mg radium tubes used for the intracavitary application.

The roentgen treatment was usually given over four rectangular facial fields, two medial and two lateral, with the beam directed through the center of the tumour (Diagram 2 a). The vertical extension of the fields was adapted to the extension of the tumour, though in most cases the upper margin ran immediately above the eyebrow and the lower one at the level of the upper lip. The voltage was about 180 kV; the filter 0.5 mm Cu or Thoraeus filter; target—skin distance from 50 to 60 cm; intensity about 50 r/minute. As a rule one field was treated daily with a dose of from 400 to 500 r, measured on the skin. If secondary infection and purulence were present at the outset, or if the patient had been in a poor general condition, smaller doses were used at the beginning and then, if possible, progressively increased. Lead screens about 3 mm in thickness were applied over the eyes in treatment of the medial fields, though on the tumour side, as a rule, not until about 1,000 r had been

given over that field. If the orbit, too, showed tumourous infiltration, a lead screen was not used over the eye on the involved side.

To judge from squamous cell carcinomas in other situations (hypopharynx, oral cavity, skin, etc.), an optimal tumour dose should lie around 6,000 r over 30 days in the event of radiotherapy alone. Determinations with ionization chambers in a wax-filled cranium (HULTBERG and THORAEUS) have shown that with a prescribed skin dose of 3,000 r per field, a tumour dose varying between 6,000 and 7,000 r is obtained in different parts of the maxillary sinus. In tumours of the paranasal sinuses and nasal cavities that are not unduly extensive, a satisfactory tumour dose can definitely be attained with the technique used here. In more extensive tumours the posterior portions of the growth must be expected to receive a smaller dose due to the increased distance from the skin surface. If it should be impossible to contain the tumour in each beam, then the non-homogeneousness of the dose will increase and certain low-dose areas will appear. In this series no detailed calculations were made as to the distribution of the dose in the individual cases. A prescribed skin dose of about 3,000 r on four fields over a period of from 30 to 35 days was regarded as roentgen therapy in 'full dosage'. The actual skin dose, particularly in the anterior fields, was of course considerably higher because of the additional dose from other fields.

Irradiation by this technique generally produced somewhat pronounced dry epidermitis as well as occasionally, particularly in the medial parts of the anterior fields, exudative epidermitis. Towards the end of the series there was usually a fibrinous epithelite of the mucous membranes in the nasal cavities and upper part of the oral cavity.

The other type of radiologic treatment consisted of local insertion of radium tubes in the operation cavity in conjunction with electrocoagulation. As a rule four radium tubes, each containing 50 mg radium, were used. These tubes are 10×5.4 mm in size and filtered with 0.35 mm Au and 0.3 mm Pt. To increase the distance they are also fitted with an outer aluminium case 3 mm in thickness (Diagram 2 b). The duration of application varied from three to five hours, depending on the magnitude of the preoperative irradiation. The radium tubes were usually inserted in that part of the operation cavity where the operator had felt most uncertain about the radical nature of the surgery; in most cases this was the upper posterior part of the cavity.

Technique of Surgical Treatment. The surgical treatment was preceded by examination of the heart, lungs and eyes, as well as ordinary blood and urine tests. The anaesthetic consisted of intravenous anaesthetic, supplemented by nitrogen monoxide and oxygen, which were administered through an endotracheal tube via the contralateral nasal cavity. The homolateral external carotid was ligated immediately before operation.

The operative method was the electrosurgical one as described by HOLMGREN, ÖHNGREN and others. Only in a few cases was an external incision through the skin employed; in the great majority of cases full resection of the maxilla could be carried out directly from the oral cavity. The principle was to destroy the tumour and adjacent tissues by electrocoagulation; then to remove those parts by means of suitable forceps. The operation was carried out accordingly in different stages. The extent of the tumour was judged from the clinical findings, the roentgenograms and a preceding exploratory Caldwell-Luc operation.

The ethmoid cells and the sphenoid sinus were usually evacuated surgically, but in those cases where these areas showed tumour infiltration, careful coagulation was done. If the tumour had invaded the soft tissues of the cheek, those parts were excised and the wound surface then coagulated. To ascertain the completeness of tumour removal, biopsy specimens were taken from several sites in the walls of the operation cavity. Chemotherapeutic agents or antibiotics were administered pre- and postoperatively to prevent any complications of infection.

Principles of Treatment. Between 1940 and 1945 the following method was applied fairly consistently in the treatment of *operable cases:* Following preoperative roentgen irradiation in a relatively low dose (1,000—2,000 r per field), electrocoagulation combined with insertion of radium in the operation cavity was carried out within from 4 to 6 weeks. In the last years of this period there was a tendency to increase the preoperative roentgen doses, and this trend was even more evident in 1946 and 1947, when preoperative roentgen therapy in 'full dosage' was given to an increasing extent even in primarily operable cases. But since in a fair proportion of cases no viable cancer could be demonstrated at operation, a more conservative method of treating some operable cases was adopted during this period. These cases underwent roentgen therapy in 'full dosage', and subsequent operation, only if there were later symptoms of recurrence. From 1948 to 1950 this method was almost consistently applied.

The number of patients who were treated by radiotherapy alone and by combination of radiotherapy and electrocoagulation year by year will be seen from Table 4. The frequency of operated cases during the different periods clearly demonstrates the above mentioned changes of the treatment principles:

Operated cases	1940—1945	92/191 = 48	per cent
» »	1946—1947	22/65 = 34	» »
» »	1948—1950	14/78 = 18	» »

An analysis of the cases from the different periods showed that these changes in the frequency of operated cases really were due to the treatment principles and not to changes in the frequency of technically

Table 4

Therapy in 334 Cases Treated

Year	Radiotherapy Alone	Radiotherapy and Surgery Combined	Total
1940	14	16	30
1941	19	14	33
1942	21	13	34
1943	13	15	28
1944	17	15	32
1945	15	19	34
1946	24	10	34
1947	19	12	31
1948	17	4	21
1949	15	6	21
1950	32	4	36
Total	206	128	334

operable cases. A preliminary investigation showed, however, that the results with the more conservative method probably were not as good as those with the combined radiologic and surgical method. From 1951 this latter technique has once more been employed in accordance with principles that will be outlined later on.

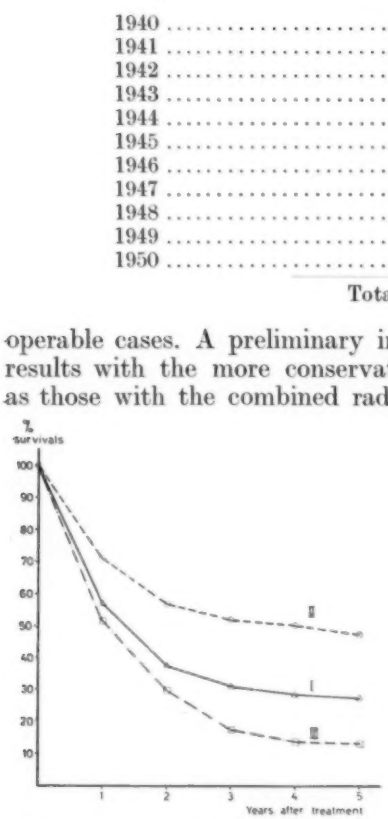


Diagram 3. Survivals. I. Total Series. II. Operatively treated cases. III. Cases treated by irradiation alone.

The *inoperable cases* were given, if possible, roentgen treatment in 'full dosage'. If the tumour showed considerable posterior spread with destruction of the base of the skull, supplementary treatment over one field behind each ear sometimes was given. Furthermore, a supplementary series with lower doses was not infrequently given over the facial fields 4 to 6 months later.

Results of Treatment

From the therapeutic point of view the patients could be classed in two main groups: those who received radiotherapy alone, and those who received a combination of surgical treatment and irradiation. The number of survivors year by year in these two groups and in the total series treated from 1940 to 1950 will be seen from Diagram 3.

In the entire treated series from 1940 to 1947 a five-years cure rate of 27 per cent was obtained. The absolute five-year cure rate during the same period was 23 per cent (Table 5).

Table 5

Five-year results in the total series

Total number of patients referred	294
Not admitted for treatment	38
Treated	256
Alive and symptom-free after five years	68
Alive with cancer after five years	3
Deaths from intercurrent disease without demonstrable cancer within five years	9
Five-year cure in the total series	68/294 = 23 per cent
Five-year cure in the treated cases	68/256 = 27 » »
Five-year cure in the treated cases from 1940 to 1945	52/191 = 27 » »

In the group which received *radiologic treatment alone* the five-year cure was 12 per cent. As this group also included some operable (but not operated) cases from 1946 and 1947 this figure is not an adequate expression for the result in only inoperable cases. During the period 1940 to 1945, when only inoperable cases were treated by radiotherapy alone, a five-year cure rate of 9 per cent was obtained (Table 6). This result imay seem poor, but it is necessary to realize that the material only ncluded inoperable advanced cases, in which the therapy from the outset was regarded as purely palliative. Some of these radiologic cures are illustrated in Figs. 1—4. Of at least equal importance, however, was the palliative value of the treatment, which can scarcely be shown in figures. In the great majority of cases the roentgen therapy brought about considerable regression of the tumour. Both swelling and any ulceration of the cheek often regressed, as likewise did growths which had invaded the oral and nasal cavities. The pain usually subsided, and the patients might obtain temporary freedom from symptoms, sometimes for a long period.

Table 6

Five-year results of radiologic treatment alone

Number of patients	142
Alive and symptom-free after five years	17 (12 per cent)
Alive with cancer after five years	1
Deaths without demonstrable cancer within five years	4
Alive and symptom-free after five years, in the series from 1940—1945	9/99 = 9 per cent.

In the series, which received *combined radiologic and surgical treatment*, a five-year cure rate of 45 per cent was obtained (Table 7). In combined radiologic and surgical treatment it is frequently difficult or impossible to evaluate the radiotherapy unless there is available a comparative series submitted to surgical treatment alone. Certain findings nevertheless

a. b. c.

Fig. 1. Female, 31, with inoperable carcinoma of left maxillary sinus. Pathologic diagnosis: Abundantly keratinizing squamous cell carcinoma. a. Severe swelling of the left zygomatic region. b. Following roentgen irradiation in a dose of about 2,500 r over four fields, there was complete regression; dry epidermitis in the irradiated fields. Subsequently a further two series of roentgen treatments were given in small doses; patient alive and symptom-free after 12 years. c. The condition after 6 years, with fairly pronounced radiation changes on the tumour side.

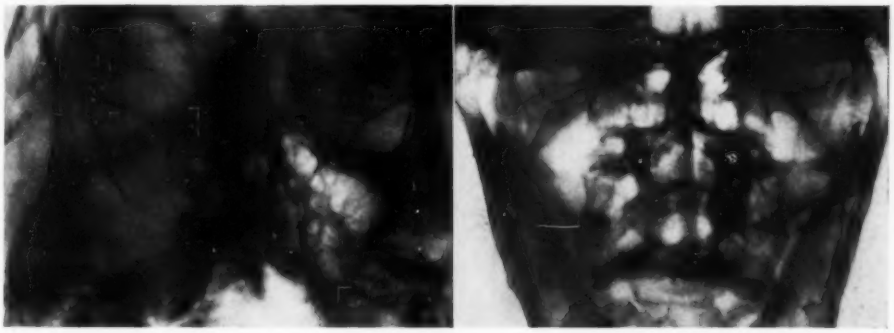
a. b.

Fig. 2. Female, 46, with carcinoma of the left maxillary sinus. Pathologic diagnosis: Squamous cell carcinoma without keratinization. a. Condition prior to roentgen irradiation. b. The tumour was highly radiosensitive and disappeared after treatment. Patient symptom-free for 7 years.

suggest that the radiologic treatment had a definite value and contributed to the good therapeutic results.

The preoperative roentgen treatment usually brought about considerable regression of the tumours, with a conspicuous reduction of the soft tissue involvement. In badly infected and purulent tumours the inflammatory component usually regressed and the growths became more circumscribed, thus facilitating the subsequent operation.

a. b.



c. d.

Fig. 3. Female, 59, with carcinoma of the right maxillary sinus. Pathologic diagnosis: Cylindric cell carcinoma. a. Swelling of right cheek. b. Healed by roentgen therapy alone, symptom-free 5 years after treatment. c, d. Extensive skeletal destruction and destruction of the great wing of the sphenoid (before treatment).

In some cases of primarily inoperable tumours, roentgen therapy in 'full dosage' made a subsequent radical operation possible. The section with a five-year observation period included nine such cases and three of these patients were alive and symptom-free after five years; in two of the cases no viable cancer was demonstrated at operation.

In 13 of the cases with a five-year observation period it became clear during the operation that radical surgery was impossible. Two of these cases were nevertheless alive and symptom-free after five years. In both cases biopsies confirmed that the operation had not been radical, and the cure had to be attributed to the postoperative radiotherapy.

The conservative method, which included roentgen therapy in 'full

a. b. c.

d.

Fig. 4. Female, 55, with carcinoma of the right maxillary sinus. Pathologic diagnosis: Keratinizing squamous cell carcinoma. a. Severe swelling of the right cheek. b. The tumour was radiosensitive and disappeared under roentgen therapy. c. The condition after 15 months. Patient alive and symptom-free after 7 years. d. Extensive skeletal destruction (before treatment).

dosage' and subsequent operation only if symptoms of recurrences appeared, was commenced in 1946 and 1947 and fairly uniformly used from 1948 to 1950. This method was suggested by HULTBERG and based on the following observations:

1. Some inoperable cases were cured by radiotherapy alone.
2. After preoperative roentgen treatment in 'full dosage' the tumours often completely disappeared. Thus 24 primarily operable cases, all

microscopically verified, received preoperative roentgen treatment in 'full dosage' and were submitted to radical operation more than two months after the radiotherapy. Notwithstanding extensive biopsies in connection with the electrocoagulation, no viable cancer was demonstrated in 11 cases.

3. By radiotherapy alone it was possible to avoid the defects unavoidable by surgical treatment.

Table 7

Five-year results of combined radiologic and surgical treatment

Number of patients	114
Alive and symptom-free after five years	51 (45 per cent)
Alive with cancer after five years	2
Deaths from intercurrent disease without demonstrable cancer within five years	5
Symptom-free five-year survivals in the series referable to 1940—1945	43/92 = 47 per cent.

A total of 42 operable cases were treated according to this method. Three patients died without signs of local recurrence. Twenty-two (52 per cent) developed manifest local recurrences. A total of 17 patients (40 per cent) were alive and symptom-free after an observation time of three to five years, 14 of them (33 per cent) without having had local recurrences during the observation time.

Table 8

Comparison between the results during different periods

	Living free from symptoms after 3 years	
	1940—1945	1946—1950
Total series	58/216 = 27 %	35/163 = 21.5 %
Total series treated	58/191 = 30.5 %	35/143 = 24.5 %
Combined treatment	46/92 = 50 %	13/36 = 36 %
Pure radiologic treatment	12/99 = 12 %	22/107 = 20.5 %
'Operable' cases	46/92 = 50 %	27/70 = 38.5 %
'Inoperable' cases	12/99 = 12 %	8/73 = 11 %

It is of interest to compare the results from 1940—1945, when all the operable cases were operated upon, with the results from 1946—1950 (Table 8). The three-year cure rate for the first period was 30.5 per cent and for the last period 24.5 per cent. The frequency of cures among the cases treated with radiotherapy alone was considerably higher during the last period mainly due to the fact that this group during

the last period included much more favourable cases. If the cases were grouped as 'operable' and 'inoperable' according to the same principles as were used from 1940—1945, the first period included 92/191 = 48 per cent and the last period 70/143 = 49 per cent 'operable' cases. The results in the 'inoperable' groups were about the same, 11—12 per cent, three-year cures for both periods. Of the 'operable' cases 50 % from the first period and 38.5 % from the last period lived symptom-free after three years. It seems highly probable that the combined radiologic and surgical treatment used from 1940—45 gave better results than the more conservative method later used. To the credit of the conservative method it may be said, that this method gave more radiologic cures without the defects unavoidable by surgical treatment. This method gave also very valuable informations about the possibilities for radiotherapy alone in these tumours and the result supports the view, that radiotherapy is of definite value also in operable cases. Some operable cases may be cured by surgery alone and some by radiotherapy alone. These two groups are probably only partly identical, and we believe that the total results are improved by the uniform use of both methods in all operable cases.

Complications of Treatment

Thirteen of the operated patients (11 per cent) died during the postoperative course. The commonest cause of death lay in cerebral complications, which occurred in six cases (meningitis, abscess of the brain).

Certain late changes due to the radiotherapy were unavoidable. The cutaneous lesions, even after the highest doses, were as a rule relatively insignificant, being limited to moderate atrophy and small teleangiectatic areas. Greater practical significance was attached to the mucosal lesions; at all events, there was a pronounced atrophy of the nasal mucous membrane following the major roentgen doses. Milder symptoms consisting in a sensation of dryness as well as crust formation were the rule; in some cases there were also more severe symptoms in the form of atrophic rhinitis. According to the case records, five (10 per cent) of our patients who lived five years or more had unilateral cataract. The radiotherapy was sometimes followed by skeletal changes with decalcification, which, roentgenologically, could not be distinguished from tumourous destruction. That these lesions were really due to the irradiation was illustrated best by the fact that such decalcification could sometimes be observed in the walls of the contralateral maxillary sinus. In most cases where these changes were found, exploratory operations were done, partly for purposes of drainage and partly to verify, by biopsy, the benign nature of the process.

a. b.

Fig. 5. Male, 60, with carcinoma of the left maxillary sinus. Treated by preoperative roentgen irradiation, electrocoagulation and insertion of radium tubes. Following sequestration there was a defect of the cheek (a), which was later corrected by plastic surgery (RAGNELL) (b). Patient alive and symptom-free after 8 years.

It is sometimes asserted that healing of the operation cavity will be delayed if preoperative roentgen therapy has been given. In the present series we gained the impression that healing was not substantially delayed, provided the operation was performed within 1—2 months after irradiation, *i. e.*, before any really pronounced fibrotic and vascular changes had developed. In those cases, on the other hand, that were not submitted to operation until long after full roentgen therapy, slower healing often occurred.

In the subsequent course there was sometimes a protracted distressing condition, with sequestration attended by periods of infection and suppuration in the involved area. Such a course occurred in 16 of the present cases. During periods of exacerbation and pain, treatment with antibiotics was found to be of value. Since the sequestra were clearly demarcated roentgenologically, open sequestrotomy could expedite healing.

Another relatively common complication in the subsequent course lay in attacks of erysipelas, the infection spreading from an infected operation cavity or a fistulous area to the skin, which was predisposed on account of the roentgen irradiation. These attacks usually subsided quite rapidly following chemotherapy or the administration of antibiotics.

Certain defects were generally unavoidable following the operation.

a. b.

Fig. 6. Male, 54, with carcinoma of the right maxillary sinus. a. Defect following electrocoagulation; b. Connected by facial prosthesis. Patient alive and symptom-free 9 years after the operation.

The commonest was a palatal defect on the same side as the tumour. Only in a few cases was it possible to spare the hard palate. This defect was corrected by a suitable denture when healing was complete, and as a rule it subsequently caused relatively little distress. Sometimes, due to the extent of the tumour, an external defect could not be avoided (excavation of the orbit, resection of soft tissues in the face). In other cases external defects arose later due to ocular complications leading to enucleation (7 cases) or due to necrosing of buccal soft tissues with poor nutrition, or fistulas developed from areas of sequestration. In some of these cases the defect could be corrected by plastic surgery (Fig. 5); in others a good prosthetic technique made social intercourse possible without embarrassment (Fig. 6). Eleven (21 per cent) of the present patients who were alive after five years had had external defects, which in five cases were corrected by plastic surgery.

Some Factors of Prognostic Importance

Metastases. It is a general observation that lymph-node metastases have a relatively low incidence in cancer involving this region compared with for instance cancer of the oral cavity. In the present series of treated patients lymph-node metastases were present on admission in 35 patients (10 per cent), if only histologically verified or clinically undoubted metastases were included. A total of 76 cases (23 per cent)

developed lymph-node metastases and 34 cases (10 per cent) developed generalized metastases during the whole observation time.

The cases which had lymph-node metastases on admission had a very poor prognosis as will be seen from the following comparison:

Cases with	lymp-node metastases, five-year cure	2/27 = 7.5	%
Cases without	» » » »	66/229 = 29	%

In the cases which had lymph-node metastases on admission or developed them later on, a 'neck dissection' was done in a total of 14 cases, usually after preoperative irradiation treatment (roentgen or teleradium). Of the patients in whom lymph-node metastases were removed, ten have a five-year observation period, and five of these were symptom-free after that period. No proof was obtained in the present series, that the lymph-node metastases could be definitely cured by radiotherapy alone. This treatment nevertheless had a good palliative effect in many cases and had probably also a definite value as preoperative treatment in the operable cases.

The mode of treatment of lymph-node metastases was, of course, frequently dependent on the behaviour of the primary tumour. If the latter failed to heal, then radical removal of the metastases would have been of little avail. In the case of an operable primary tumour associated with operable lymph-node metastases, radical 'neck dissection' after preoperative irradiation treatment was regarded as the most advisable alternative. Removal of operable lymph-node metastases was also done in a few cases of inoperable primary tumours where irradiation appeared to have brought about healing of the primary tumour.

Histologic findings. The histologic character of these carcinomas has been described in detail by RINGERTZ, among others. In the present series all the microscopic slides were examined by REUTERWALL or SANTESSON at the Radiopathologic Institute, and the following analysis was based on their reports. The frequency of the different histologic types will be seen from Table 9.

The grouping in Table 10 was done with the aim of ascertaining whether the histologic picture provided any guidance in the determination of the prognosis. Both the incidence of regional and generalized metastases and the five-year results point to a fundamental difference in degree of malignancy between different histologic types. The poorly differentiated or undifferentiated carcinomas showed the highest incidence of metastases and the poorest prognosis, and the cylindric cell carcinomas the lowest incidence of metastases and the best prognosis.

Adenocarcinoma occupied a special position from several points of view. All the tumours were localized to the ethmoid or the upper part of the nasal cavity. They grew very slowly and showed a pronounced tend-

Table 9

Histopathologic Diagnosis

Squamous cell carcinoma, well-differentiated	156
» » » , poorly differentiated	60
Cylindric » »	25
» » » with squamous cell metaplasia	9
Unspecified, undifferentiated carcinoma	52
Adenocarcinoma	11
No pathologic diagnosis available	21
Total	334

Table 10

	No. of Cases	Total Metastases	Lymph-node Metastases	Generalized Metastases	Five-year Cures
Cylindrical cell carcinoma	34	15 %	15 %	0 %	9/25 (36 %)
Well-differentiated squamous cell carcinoma ..	156	23 %	21 %	3 %	39/124 (31 %)
Poorly differentiated and undifferentiated carcinoma	112	42 %	29 %	20 %	18/78 (23 %)
Adenocarcinoma	11	0 %	0 %	0 %	2/10

ency to recur, sometimes after long symptom-free periods. Metastases did not appear but the prognosis was bad probably due to the unfavourable situation.

Situation and extension of the primary tumour. Tumours infiltrating the nasopharynx, the base of the skull or the pterygoid process were usually regarded as inoperable and had, as would be expected, a poor prognosis. Of 50 five-year observed cases with destruction of the base of the skull only 5 (10 per cent) and of 48 cases with infiltrations in the nasopharynx only 3 (6 per cent) lived symptom-free after five years.

It seemed probable that tumours situated in the upper and posterior part of the paranasal and nasal region might be more difficult to operate upon radically and at an earlier state infiltrate tissues, rendering a radical operation impossible. This led ÖHNGREN to the construction of a 'Malignancy plane', dividing the tumours in those situated in the lower, anterior region and those situated in the upper, posterior region. On account of the extension of the tumours we found it difficult in most cases to carry out this classification. It was nevertheless of great interest to study the influence of some topographic factors on the prognosis.

Tumours with roentgenologic signs of destruction in the ethmoid or the posterior wall of the maxillary antrum were sometimes regarded as doubtfully operable on account of the difficulties in removing the

Table 11

Total series treated	Five-year cure
Destructions of the ethmoid and/or the posterior wall of the maxillary antrum	41/170 = 24 %
Other cases	27/86 = 31 %
Operated series	
Destructions of the ethmoid and/or the posterior wall of the maxillary antrum	30/61 = 49 %
Other cases	21/53 = 40 %

Table 12

Relation of the tumours to the oral cavity. Prognostic importance

Total series treated	Number of cases	Lymph-node metastases on admission	Lymph-node metastases Total	Five-year cure rate
Oral cavity not involved...	171	4 %	17 %	41/126 = 33 %
Non-ulcerated tumour bulge in the oral cavity	108	10 %	23 %	19/85 = 22 %
Ulcerated tumour	55	29 %	38 %	8/45 = 18 %
Operated series				
Oral cavity not involved...	70	1.5 %	13 %	31/61 = 51 %
Non-ulcerated tumour bulge	40	10 %	10 %	16/37 = 43 %
Ulcerated tumour	18	22 %	28 %	4/16 = 25 %

tumours with sufficient margin. No great difference was found, however, between the results in the cases with and without roentgenologic destructions in the ethmoid and/or the posterior maxillary wall either in the total series or in the operated series (Table 11), and the same was true when either of these factors was tested alone. Roentgenologic destructions of the ethmoid or posterior maxillary wall may thus *per se* in no way be regarded as contraindication to operation.

Another factor of interest was the relation of the tumour to the oral cavity. As will be seen from Table 12, there was a pronounced correlation between the degree of oral involvement and the prognosis. Tumours not involving the oral cavity had the best prognosis and tumours with ulceration into the mouth the worst prognosis; for tumours invading the oral cavity but not yet ulcerated the figures lay between these extremes. There was also a striking difference in the frequency of lymph-node metastases. (Table 12.) These differences may be due to the fact that tumours with involvement of the oral cavity generally represented more advanced cases. They may, however, also be due to differences between the lymphatic system in the naso-sinusal region and the oral cavity. It is a general observation that paranasal carcinomas show a lower frequency of lymph-node metastases than oral carcinomas. When

a paranasal carcinoma has invaded the oral cavity, it may probably behave like an oral carcinoma as regards its metastasizing properties.

Recurrences. In 31 cases (27 per cent) of the operated series a local recurrence developed. Twelve of these cases were reoperated upon and of these one was alive and symptom-free after 5 years and one after 3 years. In all the other cases it was impossible to eradicate the tumours.

Results from Other Clinics

Direct comparisons with therapeutic results reported from other clinics are often impossible on account of differences in the composition of the materials. As regards the paranasal and nasal carcinomas the difficulties are unusually large. In some reports tumours of the maxillary antrum and tumours of the oral cavity with secondary involvement of the maxillary bone are included in the same group and in some materials cases of sarcomas and malignant mucous- and salivary gland tumours are included. Some reports refer only to operable cases.

Table 13

	No. of Cases	Material	Five-year Cures
Öhngren (1933)	45	Operable cases	33 %
Houser (1933)	21	» »	13.3 %
New (1935)	141	» »	37.5 %
Watson (1942)	94	Total series	20.5 %
Windeyer (1944)	69	Radiologic	18.8 %
	13	Operative	25 %
Wille (1947)	162	Total series	9.9 %
	33	Operative	18.1 %
Tod (1948)	68	Radiologic	24 %
Dargent (1948)	56	Operative	21.7 %
Present series (1953)	256	Total series	27 %
	114	Radiologic and operative in combination	45 %

In Table 13 the therapeutic results from certain reports are shown in order to give a rough idea about the results obtained in other clinics. No direct comparison with the results obtained in the present series is possible for reasons mentioned above.

Present Principles of Treatment

Partly because of experience with this series, the following therapeutic technique has been consistently employed at Radiumhemmet since 1951.

Every individual case is initially evaluated jointly by an otologist

and a radiologist with respect to operability. Each case is submitted to a biopsy, in carcinoma of the maxillary sinus, usually by a Caldwell-Luc operation. In all cases a broad communication is established between the maxillary sinus and the oral cavity at the Caldwell-Luc operation for the purposes of drainage and to make adequate inspection during the further course of treatment possible.

Those cases which are considered operable receive preoperative roentgen irradiation in accordance with the technique described in the foregoing — with from 2,000 to 2,500 r per field — and are submitted to radical operation four to six weeks later. At the same time radium tubes are inserted in the operation cavity.

The clearly inoperable cases and the borderline cases receive roentgen irradiation with about 3,000 r per field. A small number of these may in this way be rendered operable, but before any radical surgery is performed an exploratory operation with removal of extensive biopsy specimens is performed so as to verify that a viable cancer is still present.

Of primary importance to good therapeutic results in cancer of the paranasal sinuses and nasal cavities is close co-operation between the otologists and the radiotherapists. As these tumours are relatively rare it seems advisable to concentrate the treatment to centers, where sufficient experiences can be collected.

SUMMARY

The present investigation relates to 379 cases of carcinoma of the paranasal sinuses and nasal cavities, treated during the period from 1940 to 1950 at Radiumhemmet and the Otolaryngologic Department, Karolinska Sjukhuset, Stockholm. A report is presented on the symptomatology, therapeutic technique and results of treatment.

The following five-year results were obtained: Absolute five-year cure rate, 23 per cent; relative five-year cure rate, 27 per cent; all surgically treated cases (electrocoagulation in combination with radiotherapy), 45 per cent; cases subjected to radiologic treatment alone (largely inoperable cases), 12 per cent.

ZUSAMMENFASSUNG

Die vorliegende Untersuchung umfasst 379 Fälle mit Karzinomen der paranasalen Hohlräume und der Nasenhöhlen, die während des Zeitraumes 1940—1950 im Radiumhemmet und in der Hals-Nasen-Ohrenklinik des Karolinska Sjukhuset in Stockholm behandelt worden sind. Ein Bericht über die Symptomatologie, die Behandlungstechnik und die Behandlungsresultate wird vorgelegt.

Folgende 5-Jahresheilungen wurden erreicht: Absolute Heilung in 23 %; relative 5-Jahresheilung in 27 %; sämtliche chirurgisch behandelten Fälle (Elektrokoagulation in Kombination mit Radiotherapie) in 45 %; ausschliesslich radiologisch behandelte Fälle (überwiegend inoperable) in 12 %.

RÉSUMÉ

Les présentes recherches portent sur 379 cas de cancer des sinus paranasaux et des fosses nasales, traités entre 1940 et 1950 au Radiumhemmet et dans le Service d'Oto-

rhino-laryngologie, Karolinska Sjukhuset, Stockholm. Les auteurs rendent compte de la symptomatologie, de la technique et des résultats du traitement.

Les résultats au bout de cinq ans ont été les suivants: guérison complète de cinq ans, 23 pour cent; guérison incomplète de cinq ans, 27 pour cent; pour l'ensemble des cas traités chirurgicalement (électrocoagulation associée à la radiothérapie), 45 pour cent; cas traités uniquement par la radiothérapie (cas nettement inopérables) 12 pour cent.

REFERENCES

Ackerman, L. V. and del Regato, J. A.: Cancer. Mosby, S:t Louis 1947.

Berven, E.: Radiologische Behandlung. Nordischer Kongress für Otolaryngologie, Helsingfors 1926.

— Die Bedeutung der Elektroendothermie für die Strahlenheilkunde. Handb. d. ges. Strahlenheilk. 11 (1931), 1040.

— Development of technique and results of treatment of tumors of the oral and nasal cavities. Am. J. Roentgenol. 28 (1932), 332.

Capps, F. C. W. et al.: Discussion on malignant disease of the nasal cavity and sinuses. Proc. Roy. Soc. Med. 43 (1950), 665.

Dalley, V. M.: Radiation treatment of cancer of the upper jaw. Paper read at the seventh international congress of radiology, Copenhagen 1953.

Dargent, M., Gignoux, M. and Geillard, J.: Le traitement des tumeurs malignes primitives du maxillaire supérieur. Masson, Paris 1948.

Holmgren, G.: Erfahrungen über chirurgische Behandlung von malignen Oberkiefertumoren. Acta oto-laryng. 7 (1925), 511.

— Die malignen Oberkiefertumoren. Nordischer Kongress für Otolaryngologie, Helsingfors 1923.

— Diagnose, Behandlung und Prognose der malignen Oberkiefertumoren. Ztschr. f. Laryng. 16 (1928), 8.

Hultberg, S. and Thoreus, R.: Personal communication.

Houser, K. H.: Diagnosis and treatment of primary malignant neoplasms of the maxillary sinus. Arch. Otolaryng. 18 (1933), 643.

New, G. B.: Malignant tumors of the antrum of Highmore. Arch. Otolaryng. 4 (1926), 201.

— The treatment of malignant tumors of the upper jaw and antrum. Surg. Gynec. Obst. 61 (1935), 706.

Paterson, R.: The treatment of malignant disease by radium and X-rays, p. 258. Arnold & Co., London 1948.

Ringertz, N.: Pathology of malignant tumors arising in the nasal and paranasal cavities and maxilla. Acta oto-laryng. Suppl. 27 (1938).

Schall, L. A.: Malignant tumors of the nose and nasal accessory sinuses. J. A. M. A. 137 (1948), 1273.

v. Seemen, H.: Allgemeine und spezielle Elektrochirurgie. Julius Springer. Berlin 1932.

Tod, M. C.: The treatment of cancer of the maxillary antrum by radium. Brit. J. Radiol. 21 (1948), 270.

Ward, G. E. and Hendrick, J. W.: Tumors of the head and neck. Williams & Wilkins, Baltimore 1950.

Watson, W. L.: Cancer of paranasal sinuses. Laryngoscope 52 (1942), 22.

Wilk, C.: Malignant tumours in the nose and its accessory sinuses. Acta oto-laryng. Suppl. 65 (1947).

Windeyer, W. B.: Malignant tumors of the upper jaw. Brit. J. Radiol. 7 (1943), 362.

Öhngren, L. G.: Malignant tumours of the maxillo-ethmoidal region. Acta oto-laryng. Suppl. 19 (1933).